

CORRELATION BETWEEN SEVERITY OF ALCOHOL DEPENDENCE WITH AGE OF ONSET AND FAMILY HISTORY

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CERTIFICATE

This is to certify that the dissertation titled, **“CORRELATION BETWEEN SEVERITY OF ALCOHOL DEPENDENCE WITH AGE OF ONSET AND FAMILY HISTORY”**, submitted by **Dr. HARIHARAN. P**, in partial fulfillment for the award of the MD degree in Psychiatry by the Tamil Nadu Dr. M.G.R. Medical University, Chennai, is a bonafide record of the work done by him in the Institute of Mental Health, Madras Medical College during the academic years 2010 – 2013.

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DECLARATION

I, **Dr. P. HARIHARAN**, solemnly declare that the dissertation titled, “**CORRELATION BETWEEN SEVERITY OF ALCOHOL DEPENDENCE WITH AGE OF ONSET AND FAMILY HISTORY**” has been prepared by me, under the guidance and supervision of **Dr. R. JEYAPRAKASH** M.D., D.P.M., Professor of Psychiatry, Madras Medical College. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any other University board either in India or abroad.

This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulation for the award of M.D degree **Branch – XVIII (Psychiatry)** to be held in April 2013.

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LIST OF ABBREVIATIONS

FH	=	FAMILY HISTORY
FHD	=	FAMILY HISTORY DENSITY
AOO	=	AGE OF ONSET OF ALCOHOL USE
EAOO	=	EARLY AGE OF ONSET OFALCOHOLISM
LAOO	=	LATE AGE OF ONSET OF ALCOHOLISM
SADQ	=	SEVERITY OF ALCOHOL DEPENDENCE
AUDIT	=	ALCOHOL USE DETECTION INVENTORY TEST
SCAN	=	SCHEDULE FOR CLINICAL ASSESSMENT IN NEUROPSYCHIATRY
FIGS	=	FAMILY INTERVIEW FOR GENETIC STUDIES
EDSS	=	EDINBURGH DEPENDENCE SEVERITY SCORE
ADS	=	ALCOHOL DEPENDENCE SYNDROME
FTQ	=	FAMILY TREE QUESTIONNAIRE
MAST	=	MICHIGAN ALCOHOLISM SCREENING TEST
SMAST	=	SHORT MICHIGAN ALCOHOLISM SCREENING TEST
AUI	=	ALCOHOL USE INVENTORY
ADS	=	ALCOHOL DEPENDENCE SCALE
FHQ	=	FAMILY HISTORY QUESTIONNAIRE
FPA	=	FAMILY PATTERN OF ANALYSIS
SFQ	=	SOCIAL FUNCTIONING QUESTIONNAIRE
TLFB	=	TIME LINE FOLLOW BACK
BCL	=	BEHAVIOR CHECK LIST
AUDADIS	=	ALCOHOL USE DISORDER & ASSOCIATED DISABILITY INTERVIEW SCHEDULE.
CIWA-AD	=	CLINICAL INSTITUTE OF WITHDRAWAL ASSESSMENT FOR ALCOHOL

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INTRODUCTION

Alcoholism is one of the most threatening of present health problems in most of the countries. It has led to enormous burden on health care facilities and nations economy. The Global Burden of Disease Project estimated alcohol to be responsible for 1.5% of all deaths and 3.5% of the total Disability Adjusted Life Years (DALYs)¹. Epidemiological studies in India have shown a prevalence of 16-50 % rate for alcoholism, even though India is considered to be a “Dry” culture.²

Lewis et al³ (1983) demonstrated that male sex; antisocial personality and family history of alcoholism increased the risk of severity of alcoholism. Genetic studies have found a three to four fold increased risk for severity of alcohol related problems in close relatives of alcohol patients. When compared to general population, alcoholics have significant family history of alcoholism. First degree relatives of alcoholics have four fold increased risk and second degree relatives have two fold increased risk of alcoholism when compared to general population. Subjects with positive family history of alcoholism had an increased severity of alcohol- related problems; however, it was difficult to say whether this propensity is genetic or environmental or a combination of the two⁴.

The twin studies originally proposed by Francis Galton compared identical twins with fraternal twins in which one of the twins had alcoholism and found that monozygotic twins were significantly concordant with regard to the quantity of alcohol consumed. . The twin studies complemented by the adoption studies have shown that alcoholism is heritable, but the pattern of inheritance was not a simple one, it was complex and multifactorial in nature.^{5,6}

The studies done internationally⁷ indicate that alcoholism is more severe when familial. Also there is evidence that the familiarity also impacts on the AGE OF ONSET⁸. Additionally, it is established that the younger the AOO more severe the alcoholism⁹. This has lead to further explorations into what is inherited^{10,11} and what mediates the heightened severity in familial Alcoholism¹². While a few Indian studies^{13,14,15} have done similar explorations, the relationship per se amongst Familiarity, Age of Onset and Severity of Alcoholism.

REVIEW OF LITERATURE

Alcoholism is a multi-factorial psychiatric disorder, with both psychosocial and biochemical/genetic factors manifesting in individual. Studies on severity of alcohol use initially focused on Socio economic issues¹⁶. Later this was related to a variety of psychological aspects like stress and nervousness¹⁷. Severity of use was also seen to correlate with socio-cultural aspects as seen by Jellinek's classification¹⁸. Later studies noted severity of alcoholism to run in families. In fact, this has been known since ancient times. Aristotle, Plutarch and many others have commented on the familialness of alcoholism.

The twin studies originally proposed by Francis Galton compared identical twins with fraternal twins in which one of the twins had alcoholism. Certain assumptions were made in these studies, that is the monozygotic and dizygotic twins differed with their genetic makeup and the environment was similar for both the members. A study by Kaij in Sweden in 1970 found that the concordance rate for alcohol abuse was 58% for the monozygotic Twins and 28% for dizygotic Twins⁵.

Partenen et al in their Twin study in Finnish found a significant concordance in terms of frequency and amount of alcohol consumption

and abstinence in the monozygotic than in the dizygotics. This method points to genetic inheritance.⁶

Another approach is to separate “nature” from “nurture” and study individuals separated from their biologic parents soon after birth; raised by non-related foster parents and to compare them on the basis of various aspects of the alcohol abuse. The extent to which the adoptee resembled their biological parents is a direct measure of the genetic influence, while the degree to which they resemble their adoptive parents is a measure of the influence of the family environment. Major adoption studies done in Denmark and Sweden have shown that genetic factors play important role. The pattern of drinking in individuals vary depends on various combinations of genetic and environmental factors.¹⁹ Subsequent studies from other countries also have shown that children born to alcoholic parents but adopted during infancy were at a greater risk for alcoholism than adopted away children born to non-alcoholic parents²⁰.

The Twin and Adoption studies have shown that alcoholism is heritable. However the pattern of inheritance is not a simple one, it is complex and multi- factorial in nature. These studies led to changes in classification and sub grouping of alcoholism. Jellinick¹⁸ differentiated

between individuals who had persistent alcohol seeking behaviour and others who could abstain from alcohol for longer periods but were unable to control once they have started.

Cloninger developed a typological system which was initially based on alcohol related symptoms and patterns of inheritance in adoptee; later he included the personality traits in the system. He classified alcoholics into two types. Type 1 were characterized by (1) high reward dependence (one who is eager to help others, emotionally dependent, warmly sympathetic, sentimental, sensitive to social cues and persistent), (2) high harm avoidance (cautious, apprehensive, pessimistic, inhibited, shy and susceptible to fatigue) and (3) low novelty seeking (who is rigid, reflective, loyal, orderly and attentive to details). These individuals behaviourally are identified by frequent loss of control, guilt, fear about alcohol dependence and are more likely to be binge drinkers and seldom-experienced alcohol related problems before the age of 25.

These individuals were at an increased risk for alcoholism only if a provocative environment was present. They were referred to as “milieu-limited”. Most of them in this group were found to be women. In contrast, Type 2 alcoholics had characteristic of (1) high novelty

seeking (impulsive, exploratory, excitable, disorderly and distractible) (2) low harm avoidance (confident, relaxed, optimistic, uninhibited, carefree and energetic) (3) low reward dependence (socially detached, emotionally cool, practical, tough minded, and independently, self-willed). These individuals frequently encountered legal problems, accidents, inability to abstain alcohol and significant alcohol related problems before the age of 25. Males predominated in this group and found that the risk of developing alcoholism was nine times more than the general population. This group were referred as “male-limited”¹². While familial alcoholism being severe has been recognized for a much longer period, Cloninger’s work brought heightened focus on the aspect of Age of Onset and its relationship to severity of Alcoholism and Outcome.

There is a large literature looking into a biological markers or endo-phenotypes for alcoholism. Some of the important markers studied include Enzymatic markers, Electro-physiological markers and Neuro-chemical markers.

Enzymatic markers:

They include Platelet monoamine oxidase (MAO) activity, erythrocyte aldehyde dehydrogenase (ALDH) and Adenyl cyclase (AC). Platelet monoamine oxidase (MAO) activity is the most commonly studied marker and was found to be low in alcoholism 21. There is also a significant association between low MAO activity and type 2 alcoholism.²²

Electrophysiological markers

The overall EEG responses to alcohol challenges have been examined, and a hypothesis of greater EEG response to alcohol predicting later development of alcoholism was developed¹¹. Event-related potentials (ERPs), most notably the P3 wave, in response to visual and auditory evoked potentials, have been studied in risk groups for alcoholism as potential markers for risk by a number of different groups of investigators. Studies on adults with positive family histories of alcoholism, tested without ethanol ingestion, have reported both a significant diminution in P3 amplitude in some studies^{23,13}.

Neurochemical markers:

Gianoulakis et al. (1989) found lowered β -endorphin levels in non-alcoholic subjects with strong family histories of alcoholism (high risk), relative to those with no family history of alcoholism (low risk), and also in alcoholics who had been abstinent for at least 6 months.²⁴

This review would however focus more on studies, which explore family history, Severity and Age of onset in alcoholism.

1. Studies looking at severity with particular focus on its relationship with family history.
2. Studies looking at severity of alcohol dependent and age of onset of alcohol use.
3. Indian studies exploring issues related to severity of alcohol dependence, familiarity and age of onset along with critical evaluation.

**TABLE. 1. STUDIES LOOKING AT SEVERITY WITH
PARTICULAR FOCUS ON ITS RELATIONSHIP
WITH FAMILY HISTORY**

STUDY	DESIGN & SUBJECTS	IMPORTANT FINDINGS
Frances et al ⁷ 1984	<ul style="list-style-type: none"> • 2215 Navy recruits from Alcoholism rehabilitation program. • Self reported biological questionnaire. Familial analysis was blinded. 	<ul style="list-style-type: none"> • More the no. of first degree relatives, worse the outcome of alcoholism at different points of time.
Penick et al ²⁵ 1987	<ul style="list-style-type: none"> • Multicenter study of subjects from Alcoholism treatment center. • Structured interview was done. • 568 men with a mean age of 47 yrs. • Reliability was established by giving FH questionnaire on 2 separate occasions 2-4 weeks apart and confirmed in 35 alcoholics. 	<ul style="list-style-type: none"> • 65% were FHP and had significantly more medical problems than FHN. • FHP subjects were associated with AOO and increased severity.
Worobec et al ²⁶ 1990	<ul style="list-style-type: none"> • 265 male ADS subjects in a alcohol rehabilitation programme. • FTQ, MAST, AUI & ADS were administered in a group format. • FH only from the subject; not corroborated with other family members. • For FHP only parental alcoholism was taken. 	<ul style="list-style-type: none"> • 149 were FHP. • FH had statistically significant correlation with AOO and Severity • Parental alcoholism was a significant predictor of alcoholism.
Schachter et al ²⁷ 1990	<ul style="list-style-type: none"> • 120 male and female ADS subjects alcoholism clinics and General Hospitals. 	<ul style="list-style-type: none"> • None of the association was statistically Significant

	<ul style="list-style-type: none"> • Short MAST, SADQ & FHQ used. • Reliability of information from other sources not provided 	
Hasin & Glick ²⁸ 1992	<ul style="list-style-type: none"> • 43809 respondents to a nation wide survey using the National Health interview. • Severity checked by the no. of criteria met for the DSM 3R. 	<ul style="list-style-type: none"> • 10% with mild dependence 18% in the moderate group and 24% in the severe group had their first drink before 15yrs. • 29% in the mild dependence, 33.3% in the moderate group and 46% in the severe group had a FHP
Dejong & Roy ²⁹ 1993	<ul style="list-style-type: none"> • 249 consecutive male subjects from a alcoholic clinic were interviewed using unstructured interview. • MAST was used for Severity 	<ul style="list-style-type: none"> • FHP was significant associated with AOO and severity.
Grant et al ³⁰ 1994	<ul style="list-style-type: none"> • National Longitudinal Alcohol Epidemiological Survey. • Nationwide household survey consisting of interviews with 42,862 persons. • AUDADIS was used. 	<ul style="list-style-type: none"> • found that family history of alcoholism had a substantial effect on the development of alcohol dependence over the life span.
Keenan et al ³¹ 1996	<ul style="list-style-type: none"> • 36 ADS subjects of both the sexes from an Alcohol treatment programme. • SADQ and Family History questionnaire based on RDC was administered. • FH was divided into narrow and broad 	<ul style="list-style-type: none"> • Mean SADQ scores was 30.6 • There was no significant correlation between FH and SADQ.

Hill S.Y et al ³² 2000	<ul style="list-style-type: none"> • 175 children whose parents were part of the Cognitive and personality factors Family study were enrolled. • FH was assessed by Feigner's criteria • Severity was assessed by Adolescent alcohol involvement scale. 	<ul style="list-style-type: none"> • High risk children had EAOO and Alcohol dependence. • Also High Family density has increased risk children for alcohol initiation and impaired postural control.
Johnson et al ³³ 2000	<ul style="list-style-type: none"> • 253 ADS subjects of both the sexes offered free treatment were enrolled. • They were assessed using Self reports for AOO and alcohol profile. They were also assessed with TLFB, MAST, ASI, BCL, SFQ 	<ul style="list-style-type: none"> • Subjects less than 20yrs had earlier onset, FHP, greater duration of drinking, more alcohol related problems and legal problems.
Assanangkor nchai et al ³⁴ 2002	<ul style="list-style-type: none"> • Case control study of 91 ADS subjects and compared with 77 harmful drinkers and 144-control group from the IPD and OPD of medical, surgical and psychiatric clinics. • They were administered 1-2 hr face to "face to face" and "trilevel method" questionnaire. • Scales administered were AUDADIS and FH from the subjects only. 	<ul style="list-style-type: none"> • Significant relationship between drinking father and occurrence of harmful or ADS.

LEGEND

ADS=ALCOHOL DEPENDENCE SYNDROME; FTQ=FAMILY TREE QUESTIONNAIRE; MAST=MICHIGAN ALCOHOLISM SCREENING TEST; AUI=ALCOHOL USE INVENTORY; AD SCALE= ALCOHOL DEPENDENCE SCALE; SMAST=SHORT MICHIGAN ALCOHOLISM SCREENING TEST, SADQ=SEVERITY OF ALCOHOL DEPENDENCE QUESTIONNAIRE; FHQ=FAMILY HISTORY QUESTIONNAIRE; RDC=RESEARCH DIAGNOSTIC CRITERIA; AUDADIS=ALCOHOL USE DISORDERS AND ASSOCIATED DISABILITIES; TLFB=TIME LINE FOLLOW BACK; ASI=ADDICTION SEVERITY INDEX; BCL=BEHAVIOUR CHECK LIST; SFQ=SOCIAL FUNCTIONING QUESTIONNAIRE;IPD=INPATIENT DEPARTMENT;OPD=OUTPATIENT DEPARTMENT.

It is now well accepted that chronic alcohol drinking produces a variety of physiological and physical changes in humans. Studies over the last 100 years have demonstrated an approximate four fold increased risk for alcoholism in the first- degree relatives of alcoholics. This same risk also is observed in the dizygotic twins (who share 50% of their genes), but the risk is significantly higher in the monozygotic twins of alcoholic individuals (who share 100% of the genes)³⁵.

As shown in table 1, Frances et al in 1984 studied 2215 Navy recruits from Alcoholism rehabilitation program. They found that 50% of the samples had FAMILY HISTORY POSTIVE and more the number of first-degree relatives, worse the outcome of alcoholism at different points of time Cook & Winokur⁸ studied 156 males and 103 females Alcohol dependence subjects from the Iowa state. They used semi-structured interview and contacted the family members for the confirmation of FH. If there were no first-degree relative then close relatives of the family would be contacted and FH was be completed. First-degree relative was divided into Primary and Secondary based on the information. Secondary were defined as any First-degree relative whose psychiatric symptoms predated the alcohol use and they were excluded from the study, in order to get a

homogenous sample. They concluded that FHP group had earlier AGE OF ONSET OF USE and heavier drinking. FHP also displayed more conduct disorder, aggressive behavior and depressed mood.

Penick et al²⁵ studied 568 men with a mean age of 47 yrs in a Multicenter study of subjects from Alcoholism treatment centre in America. They used Structured interview (Psychiatric Diagnostic Interview) and trained staff for the data collection.. The reliability was established by giving FH questionnaire on 2 separate occasions 2-4 weeks apart and confirmed in 35 alcoholics. The consistency of the FH information was 96% of overall agreement across categories. The severity was assessed based on alcohol related hospitalization, arrest, job loss and separation. The basis on how AOO was defined and how the information was recorded was not mentioned. They concluded that 65% of these subjects were FHP and had significantly more medical problems than FAMILY HISTORY NEGATIVE. FHP subjects were associated with AOO and increased severity.

Schachter et al²⁷ studied 120 subjects diagnosed as Alcohol dependence syndrome admitted in a General Hospital Outpatient Alcoholism Clinic In USA. They administered SMAST, SADQ and Family History Questionnaire (FHQ). FH was assessed by FHQ, which was a self-administered questionnaire. Reliability of the

information in the FH is not mentioned. They showed that subjects with positive family history group presented with severe dependence and with greater history of police arrests than the family history negative groups but these differences did not reach conventional levels of statistical significance.

Dejong & Roy²⁹ studied 249 consecutive male subjects, who met the criteria for DSM3 alcoholism from an alcoholic clinic in USA. A research social worker administered MAST, SADS-L and an extensive set of unstructured questions to assess the alcohol use and FH of alcoholism. Familial Alcoholism was considered if alcoholism was present in biological father, paternal grandfather or paternal uncles and all others were classified as non Familial. FHP (familial alcoholism) was significantly associated with EAOO and severity.

Keenan et al³⁰ studied 36 ADS subjects (DSM 3R) of both the sexes from an Alcohol treatment programme center in Dublin. They were evaluated 14 days after abstaining from alcohol and 1 week after benzodiazepine treatment. Even though their main aim was to assess for Neurological signs and Severity of alcohol dependence syndrome by SADQ, they also collect information of FH using Family History RDC. Then FH was classified into Broad and Narrow FH. A Narrow

FH was defined as presence of alcoholism in one or more of the First-degree relatives. And Broad was defined as alcoholism in First and Second degree relatives. They found that there was no significant correlation between FH and SADQ.

Hill S.Y et al³¹ studied 175 children whose parents were part of the Cognitive and personality factors Family study in Pittsburgh. Ascertainment of High-risk families was based on presence of two male alcoholic brothers who met the criteria for alcoholism by Feigner's criteria. A structured Diagnostic Interview Schedule was performed after blinding for all living and available relatives. For those relatives not assessed by face to face interview, a minimum of two separate FH reports were used to arrive at an appropriate FH diagnosis. Severity was assessed by Adolescent alcohol involvement scale. High-risk children had EAOO and Alcohol dependence.

Johnson et al³² studied 253 ADS subjects of both the sexes in Houston. They were offered free treatment for alcoholism and recruited through newspaper advertisement. They were assessed using Self reports for AOO and alcohol profile. They were also assessed with TLFB, MAST, ASI, BCL; SFQ and personality. They concluded that the AOO was associated with greater severity of psychopathology

with diminishing AOO. The <20 years onset groups were found to have greater severity of alcohol related problems, socio-occupational disturbances, positive family history and antisocial traits.

TABLE. 2. STUDIES LOOKING AT SEVERITY OF ALCOHOL DEPENDENCE AND AGE OF ONSET OF ALCOHOL USE.

STUDY	DESIGN & SUBJECTS	IMPORTANT FINDINGS
Corrigan et al ³⁵ 1986	<ul style="list-style-type: none"> • 158 subjects from a General medical ward • MAST, CAGE, SADQ & EADS were administered. • Methodology not clear 	<ul style="list-style-type: none"> • 34.7% were found to be Alcoholics. • Medical alcoholics were less severely dependent than psychiatric ward alcoholics. • Physical withdrawal was earlier in medical ward alcoholics than psychiatric ward alcoholics • Mean SADQ was 15.1±11.9
Latcham ³⁶ 1985	<ul style="list-style-type: none"> • 193 Men & 47 Females admitted in a psychiatric hospital • Only subjects accounts of FH taken • EDSS was used for severity 	<ul style="list-style-type: none"> • One third of males and half of females had a FHP and mostly in the First-degree relative. • AOO was the best predictor of Severity • FH was the least good predictor of Severity. • None of the 3 variables predicted severity in women.
	<ul style="list-style-type: none"> • 171 alcoholics from an alcohol treatment 	<ul style="list-style-type: none"> • Mean AOO was 33.4 ± 10.9 yrs.

<p>Irwin, Schuckit & Smith³⁷ 1990</p>	<p>programme.</p> <ul style="list-style-type: none"> • Face to face interview questionnaire • Repeated with one relative. • AOO was defined as age at which subject first met the DSM3r criteria for Alcohol abuse or dependence. 	<ul style="list-style-type: none"> • 22% were EAOO and 78% were in the LAOO group. • EAOO had numerous social complications and associated with childhood criminality and other drug use.
<p>Picken et al³⁸ 1991</p>	<ul style="list-style-type: none"> • 392 Twins from a multiple substance programme and diagnosed as ADS • Written questionnaire about FH and alcohol use. • Interviewer and clinicians were blind to each other about the zygoty. • AOO was defined as “earliest age at which family, social, health, occupational & legal was affected due to use of alcohol”. 	<ul style="list-style-type: none"> • In male twins there was higher concordance rate for alcohol abuse & dependence in Monozygotics than dizygotics. • AOO & severity also correlated significantly.
<p>Lewis & Bucholz³⁹ 1991</p>	<ul style="list-style-type: none"> • 2572 Subjects from the Epidemiological Catchment area project. • Interviewed by lay examiners in the household and institutions using the NIMH diagnostic questionnaire. 	<ul style="list-style-type: none"> • 19% FHP • Gender, Antisocial personality & FH associated significantly with alcoholism. • Mean AOO in males was 18.8 ± 5 yrs and in females it was 21.8 ± 6.6 yrs.

Turner et al ⁴⁰ 1993	<ul style="list-style-type: none"> • 220 ADS subjects admitted in the alcohol rehabilitation programme. • FTQ, MAST & AUI were administered by an educational coordinator. • Clarity about information from other relatives not available. • Four methods of FH were analyzed. • AOO was defined clearly 	<ul style="list-style-type: none"> • AOO was found to be powerful predictor of alcoholism. • Family Pattern of Analysis explained more variance than dichotomy method.
Sigvardson Cloninger & Bohman ⁴¹ 1996	<ul style="list-style-type: none"> • 577 male and 660 female subjects from the original Stockholm adoption study • Extensive reliable data was collected. 	<ul style="list-style-type: none"> • Type 1 and 2 were independently heritable forms of alcoholism.
Windle ⁴² 1996	<ul style="list-style-type: none"> • 12686 men and women recruited in the National longitudinal survey of youth. • Semi-structured interviews were used in the original sample but later were correlated with siblings. 	<ul style="list-style-type: none"> • FHP had EAOO and associated with higher rates of delinquency.
Hauser. J. & Rybakowski . J., ⁴³ 1997	<ul style="list-style-type: none"> • 296 male alcoholics in whom detailed studies of family history 	<ul style="list-style-type: none"> • Early onset of dependence, familial history of psychiatric diseases, severe intensity of alcohol-related problems and high prevalence of psychiatric disturbances and somatic diseases characterized Type 3 apart from type 1 and 2.

Hill & Yuan ⁴⁴ 1999	<ul style="list-style-type: none"> • 175 subjects whose parents were part of the Cognitive and personality factors Family study were enrolled. • Diagnostic Interview Schedule was used on all living and available relatives by a M.A level interviewer. • AOO was assessed by self report scale 	<ul style="list-style-type: none"> • High risk children began drinking earlier than the others • FH of alcoholism was a predictor of alcohol use and problems in the adolescents.
Gruber et al ⁴⁵ 1996	<ul style="list-style-type: none"> • 91175 students in the 6th, 9th and 12th grade were assessed in the classroom. • AOO was assessed by a self-reportquestionnaire. 	<ul style="list-style-type: none"> • Mean AOO 14.4yrs • EAOO was associated with increased risk of initiating other drugs.
Chao Liu et al ⁴⁶ 2004	<ul style="list-style-type: none"> • Study of 3372 male-male Twin pairs based on telephone based interviews. 	<ul style="list-style-type: none"> • 38% of variation in the AOO for each symptoms on Beresford's Classification is due to addictive genetic factor. • This study supports heritability of AOO of DSM-3R defined symptoms of Alcohol dependence.
Cheng et al ⁴⁷ 2004	<ul style="list-style-type: none"> • Cohort subjects from the community were reassessed after a period of 4yrs. • Standardized semi structured interview for alcoholism was used 	<ul style="list-style-type: none"> • This study confirms the significant roles of anxiety disorders and of the ADH2*1 allele as an antecedent of alcoholism among specific age and sex groups.

Lee and Diclemente⁴⁸ and Buydens-branchey et al 49, defined early onset alcoholics as those with heavy drinking manifestations before the age of 20 years. Jellinick¹⁸ also suggested that an AOO of problem drinking less than 20 years segregated the alcoholics into various subtypes. Von Knorring and his colleagues proposed a classificatory system different from that of Cloninger based on the AOO. He divided alcoholics into type1 and type2. Type 2 alcoholic (AOO <25yrs) were found to be more aggressive and had difficulty in the work place and with law as compared with type1. But more reliance on the AOO as a criterion to classify the two groups raises the question whether this variable correlates with the clinical course as well the typology. In fact, the AOO alone has been associated with severe course of alcoholism and a higher risk of other drug abuse.

Lee and Diclemente⁴⁸ studied “the age at which a consistent pattern of heavy alcohol use was established” and “the duration of problem drinking” in 70 alcoholic outpatients (21 women) using the Alcohol Use Inventory (AUI). Alcoholics who began heavy drinking at age 20 or below reported significantly greater social role maladaptation, more loss of behavioural control when drinking, greater severity of alcoholism, more severe alcoholic deterioration, and more frequent psycho perceptual withdrawal symptoms (delirium tremens) than later-onset alcoholics. Age

of onset was consistently a better correlate of these alcoholic patterns than the duration of heavy drinking.

Grant and Dawson⁵² showed that the AOO predicted the likelihood of the adult alcohol dependence. The prevalence for individuals less than 14 years was 40% and for those 20 and older it was 10%. They also found that the abstinence at the age of 16 years was found to be a predictor of limited use at the age of 23 were regular drinking at age 16 had increased risk for heavy drinking by fourfold at the age of 23 . Hill and Yang⁴⁶ in there study made important conclusions, they are (1) high risk children begin drinking earlier than the low risk children and (2) the risk for developing alcohol dependence can be predicted by the AGE OF ONSET (Hill & Yuan, 1999)

Corrigan et al³⁵ studied 158 subjects from a General medical ward in Dublin. They were interviewed on the third or the fourth day of the admission. Selected patients were administered MAST, CAGE, SADQ AND EADS. They recruited based on inclusion and exclusion criteria. However was not very clear. 34.7% were found to be Alcoholics.

Mean SADQ was 15.1 ± 11.9 . Medical alcoholics were less severely dependent than psychiatric ward alcoholics. Physical withdrawal was earlier in medical ward alcoholics than psychiatric ward alcoholics.

Latcham³⁶ in 1985 studied 193 men and 47 women ADS subjects admitted in a psychiatric hospital in England and Scotland. They were interviewed using standardized interview methods. Only subjective accounts of FH taken were taken, no efforts to confirm the FH. One week retrospective Diary method, EDSS and time spent in hospital were used to assess severity of alcoholism. One third of males and half of females had a FHP and mostly in the First-degree relative. AOO was the best predictor of Severity. FH was the least good predictor of Severity. None of the 3 variables predicted severity in women.

Lewis & Bucholz³⁹ 2572 Subjects from the St.Louis component of Epidemiological Catchment Area project in USA. Subjects Interviewed by lay examiners in the household and institutions using the NIMH diagnostic questionnaire. There were followed up one year later and reassessed. 19% had FHP. Gender, Antisocial personality & FH associated significantly with alcoholism. Mean AOO in males was 18.8 ± 5 yrs and in females it was 21.8 ± 6.6 yrs. Details on what basis the FH and AOO were assessed was not clear.

Turner et al⁴⁰ studied 220 men who met the criteria for either alcohol abuse or ADS from an alcohol rehabilitation Center in USA. FTQ, MAST & AUI were administered by an educational coordinator. Clarity about information from other relatives was not available. Four methods of FH

were analyzed. AOO was defined clearly. AOO was found to be powerful predictor of alcoholism. Family Pattern of Analysis explained more variance than dichotomy method.

Windle⁴² studied 12686 men and women recruited in the National longitudinal survey of youth in New York. Semi-structured interviews were used in the original sample but later were correlated with siblings. Alcoholism was assessed by the quantity taken and other questionnaire such as adverse social consequences and Dependency symptoms were used. As part of the study Delinquency also was assessed. FH was assessed in subjects and their siblings were identified and FH was assessed. FH was divided into High risk if parents and grandparents had problem drinking, moderate risk if only parents were having problem drinking and low risk if no First-degree relatives had problem drinking. FHP had EAOO and associated with higher rates of delinquency.

A study by Hill & Yuan⁴⁴ studied 52 children and adolescents at low risk for developing alcoholism and 73 children and adolescents from high-risk families in the age group of 7 to 18 and followed them annually. Ascertainment Of High risk families were based on the presence of two male alcoholic brothers, with one member of the pair being in in-patient treatment for alcoholism. All the living siblings were invited to participate in the study and later DIS was administered. For severity of alcoholism and

AOO they were administered K-SADS and AAIS. They found that the High-risk children showed a significantly earlier age of onset to begin drinking (Hill & Yuan, 1999). Anderson et al⁵² found that early alcohol drinking was a beginning of a long-term large-scale consumption of alcohol. They also found that drinking alcohol at 15 yrs among males was a strong predictor of later weekly consumption of more 21 units.

A study done by Natera-Rey G et al⁵³ from a population (n = 8,890) drawn from a 1988 national survey on addictions in Mexico City's urban population revealed a prevalence of heavy drinking in 13.7% for males and 0.6% for females; Alcohol dependence in 9.9% of males and 0.6% of females. Men with positive were twice more likely to develop dependence syndrome than family history negative males.

There are many drawbacks encountered in the study of AOO. The discriminating AOO may vary across different studies. The effects related to the AOO may be confounded by illness duration. Therefore, greater severity when compared between early and late alcoholics could be an artefact of the illness duration.⁵² Robins et al⁵⁴ cautions that early onset of drinking may be an indicator of other psychiatric disorders and may not be a direct factor in subsequent problem manifestation.

Table. 3. INDIAN STUDIES EXPLORING ISSUES RELATED TO SEVERITY OF ALCOHOL USE, FAMILY HISTORY AND AGE OF ONSET ALONG WITH CRITICAL EVALUATION.

TABLE SHOWING THE SUMMARY OF INDIAN STUDIES

AUTHORS	STUDY SETTINGS AND METHODOLOGY	FACTORS STUDIED
Varma et al ⁵⁵ (1980)	<ul style="list-style-type: none"> • Rural and urban population • Verbally administered questionnaire • Studied the age of onset • No reliable informants. 	<ul style="list-style-type: none"> • They found the age of onset different age groups.
John and Kuruvilla ⁵⁶ (1991)	<ul style="list-style-type: none"> • Retrospective hospital case record analysis • Postal follow up • Assessment of Family History methodology not mentioned. • No particular Severity scale was used for the assessment alcohol related problems. 	<ul style="list-style-type: none"> • 52.5% of 200 subjects had a FHP • Those who took treatment had 72% FHP and higher alcohol related problems
Varma et al ⁵⁷ (1994)	<ul style="list-style-type: none"> • 51 male patients of alcohol dependence from the drug de-addiction clinic. • They were administered alcohol use Proforma, modified Sensation-Seeking Scale, Multiphasic Personality Questionnaire (MPQ), and a checklist of behavioural tendencies when drinking. 	<ul style="list-style-type: none"> • EOO higher FHP and alcohol related problems. • The LAOO were anxiety-prone and guilt-ridden, and had less alcohol-related problems.
Benegal et	<ul style="list-style-type: none"> • Alcohol naïve sons/male siblings of alcoholics. • Studied p300 amplitude 	<ul style="list-style-type: none"> • They found that p300 amplitude in the auditory paradigm showed significant

al ¹³ (1995)	after dividing them into FH loading based on no. of relatives were alcoholic and AOO	inter group differences between the High FH-EAOO group.
Pratima murthy et al ¹⁴ (1996)	<ul style="list-style-type: none"> Recruited 57 male in-patient Alcoholic patients and 40 male volunteers. They used a semi-structured questionnaire to collect the details of alcohol consumption, alcohol related problems and FH. Details about the method of concluding FHP and FHN were not mentioned. 	<ul style="list-style-type: none"> ALDH was significantly lowered in the alcoholics and their first-degree relatives compared to controls
Sujaya Kumara ¹⁵ 1997	<ul style="list-style-type: none"> Studied the 70 probands admitted in the deaddiction unit with ADS and divided them into EAOO and LAOO. Methodology was reliable but numbers of informants were restricted to 2 relatives. SADD was administered for severity of alcoholism, APQ for alcohol related problems and or FH used FIGS 	<ul style="list-style-type: none"> Three Methods of FH was used in this study. They include Linearity, Generational and Quantitative methods FH of Alcohol dependence was found to be significantly more in the EAOO than the LAOO. However there were no significant differences in the Severity of both the groups.
John Abraham & Chandrasekar an ⁵⁸ 1997	<ul style="list-style-type: none"> They validated the Severity of Alcohol Dependence Data (SADD) questionnaire after translating it into Tamil. They tested this instrument in 70 consecutive patients who attended the alcohol deaddiction center. 	<ul style="list-style-type: none"> final version of the modified SADD questionnaire was highly significant with the natural variables associated with severe Dependence
Sateesh Babu and Sen Gupta ⁵⁹ (1997)	<ul style="list-style-type: none"> They studied the severity of problem drinking in newly admitted patients in the wards of Medicine, Orthopaedics and General surgery. They used MAST and AUDIT as the screening 	<ul style="list-style-type: none"> 19.6% qualified for problem drinking. 10.3% were found to be Alcohol dependent according to DSM-3R. 94% of them required medical help, 92% had alcohol related problems,

	instrument and Addiction Severity index to assess the severity in all the spheres of alcohol related dysfunction.	37% required intervention for family problems, 35% had problems in the employment, 13.7% had psychiatric problems and 1.9% had legal problems.
Meena et al ⁶⁰ 2002	<ul style="list-style-type: none"> Studied 4,691 subjects aged 14 years and above in the urban area and administered WHO Questionnaire on a house-to-house basis. 	<ul style="list-style-type: none"> Family history of alcohol users in the study suggests that if there is someone using alcohol already in the family it has a strong effect at the initiation of use in the next generation.
Chandrasekaran et al ⁶² (2001)	<ul style="list-style-type: none"> Studied around 800 patients with alcohol dependence A semi-structured proforma to elicit details regarding alcohol onsumption, SADD (severity of alcohol dependence data questionnaire) and APQ (alcohol problem questionnaire) but did not elaborate on the methodology and the reliability of information collected on FH and AOO. 	<ul style="list-style-type: none"> They found that 67.1% of the patients had family history of ADS with a mean age of onset of alcohol at 23.18(±6.92). Mean SADD score of 23.95 (±9.01)
Ashu Ranjan ⁶³ 2001	<ul style="list-style-type: none"> Studied 64 male subjects using a detailed methodology for Family History, Age of Onset and Event-related potentials (auditory) 	<ul style="list-style-type: none"> Concluded that alcoholics with high Family loading have lower P300 amplitudes and early initiation of alcohol intake predisposes to early onset of dependence. Drawbacks were small sample size, no control group and use of auditory stimuli than visual because most of the auditory ERP have yielded negative results.

In India, there have been studies on alcoholism since 1970. But these studies lacked in terms of descriptions of methodology and direct studies of FH, AOO and SEVERITY. John and Kuruvilla⁵⁹ did a seven-year follow-up of 79 patients treated in their deaddiction unit. They did a retrospective hospital case record analysis and postal follow up. Even though their primary objective was not family history, they did collect the data for the same and found that 52.5% of 200 patients had a positive family history of Alcoholism. Those who took their treatment package had more family history (72%) and alcohol related problems (delirium tremens, withdrawal symptoms and alcoholic hallucinosis) compared to those who did not accept the treatment package. The methodology of the family history and the reliability is not mentioned.

Varma et al⁵⁷ studied fifty-one male patients of alcohol dependence (DSM-III-R, APA, 1987) attending the drug de-addiction clinic of a general teaching hospital in India. They were administered a composite socio-demographic and alcohol use Proforma, modified Sensation-Seeking Scale, Multiphasic Personality Questionnaire (MPQ), and a checklist of behavioural tendencies when drinking. The early-onset alcoholics (age at onset of alcohol dependence 25 years or less) were younger, had a larger proportion of first-degree relatives with both lifetime use and abuse/dependence of alcohol but not of other psychoactive

substances and they experienced a greater number of alcohol-related problems in the previous 1 year. They were also higher sensation seekers, higher on the Psychopathic deviate scale of MPQ, and tended to display aggression, violence, and general disinhibition when drinking. The late-onset alcoholics (age at onset of alcohol dependence more than 25 years) were anxiety-prone and guilt-ridden, and had less alcohol-related problems.

A study by Benegal et al¹³ studied p300 amplitude in 4 groups of alcohol naïve sons/male siblings of alcoholics. He divided the groups based on permutation of two defining characteristics (i.e. High Family History of Alcoholism and EAOO) and found that p300 amplitude in the auditory paradigm showed significant inter group differences between the High FH-EAOO group. Pratima murthy et al¹⁴ conducted a study on Erythrocyte Aldehyde Dehydrogenase as a potential marker for AD. They recruited 57 male in-patient Alcoholic patients and 40 male volunteers for the study. They used a semi-structured questionnaire to collect the details of alcohol consumption, alcohol related problems and FH. Details about the method of concluding FHP and FHN were not mentioned. They found that the ALDH was significantly lowered in the alcoholics and their first-degree relatives compared to controls. They concluded that the observed

low Erythrocyte Aldehyde Dehydrogenase in alcoholics and their first-degree relatives could be a trait marker for alcoholism.

Sujaya Kumara¹⁵ in his unpublished M.D thesis studied the 70 probands admitted in the deaddiction unit of NIMHANS, who were diagnosed as ADS and divided them into EAOO and LAOO. SADD was administered for severity of alcoholism, APQ for alcohol related problems and for FH used FIGS. Methodology was reliable but numbers of informants were restricted to 2 relatives. Three Methods of FH was used in this study. They include Linearity, Generational and Quantitative methods. FH of Alcohol dependence was found to be significantly more in the EAOO than the LAOO. The mean EAOO was 33.5yrs and 42.58 in the LAOO. However there were no significant differences in the Severity of both the groups.

A study by John Abraham & Chandrasekaran⁵⁸ in 1997 validated the Severity of Alcohol Dependence Data (SADD) questionnaire in Indian language. They tested this instrument in 70 consecutive patients who attended the alcohol deaddiction center. After eliminating 3 questions out of 15 original questions due to difficulty in translation and poor correlation of some items in the questionnaire. The questionnaire was administered in a one to one interview format to prevent questions being misinterpreted and to clarify any doubts from the patient. In conclusion the final version

of the modified SADD questionnaire was highly significant with the natural variables associated with severe Dependence. Sateesh Babu and Sen Gupta⁵⁹ had studied the severity of problem drinking in newly admitted patients in the wards of Medicine, Orthopaedics and General surgery. They used MAST and AUDIT as the screening instrument and Addiction Severity index to assess the severity in all the spheres of alcohol related dysfunction. ASI does not have a translated version of the local languages, in view of this; interview was conducted with the English version with the help of an interviewer. Out of 363 new admissions, 51(19.6%) qualified for problem drinking and were interviewed further. 36(10.3%) were found to be Alcohol dependent according to DSM-3R. Also 94% of them required medical help, 92% had alcohol related problems, 37% required intervention for family problems, 35% had problems in the employment, 13.7% had psychiatric problems and 1.9% had legal problems.

Meena et al⁶⁰ studied 4,691 subjects aged 14 years and above in the urban area. WHO Questionnaire (Alcohol and other Addictive Substance Abuse Check List) was administered to the study subjects. They conducted a house-to-house survey. They found that 94.83% respondents had their first drink between the ages of 15-25 years. Age at which alcohol users had started taking alcohol illustrated that alcohol use started at a younger age.

Singh et al. (2000) also reported similar finding. Reasons stated for initiation of alcohol use so early in life were pressure from friends or peer groups, experimentation and curiosity. In Family history of alcohol user's, father was abusing alcohol in 23.16% cases while in 7.5% cases abuse in family was present in uncle. Family history of alcohol users in the study suggests that if there is someone using alcohol already in the family it has a strong effect at the initiation of use in the next generation. This point was further strengthened by a study among child labourers of Surat city (Bansal and Banerjee⁶¹, 1993). They reported 99.5% substance abuse at work place followed by 94.3% abuse among neighbours. This high prevalence of substance abuse in the surrounding significantly prompted child labourers in their initiation of substance abuse.

Chandrasekaran et al⁶² studied around 800 patients [796 (99.5%) men and 4 (0.5%) women] with alcohol dependence over a period of 5 years from 1995 to 1999. They used a semi-structured proforma to elicit details regarding alcohol consumption, SADD (severity of alcohol dependence data questionnaire) and APQ (alcohol problem questionnaire) but did not elaborate on the methodology and the reliability of information collected on FH and AOO. They found that 67.1% of the patients had family history of alcohol-dependence syndrome with a mean age of onset of alcohol at 23.18(\pm 6.92). With a mean age of onset of daily drinking at

30.07(\pm 8.71) and with a mean SADD score of 23.95 (\pm 9.01) and majority (44.4%) of the patients belonging to the 35-44 age group. Ashu Ranjan⁶³ in 2001 for his Dissertation studied 64 male subjects using a detailed methodology for Family History, Age of Onset and Event-related potentials (auditory) and concluded that alcoholics with high Family loading have lower P300 amplitudes and early initiation of alcohol intake predisposes to early onset of dependence.

A direct study of FAMILY HISTORY OF ALCOHOLISM (FHA), AGE OF ONSET (AOO) and SEVERITY OF ALCOHOL DEPENDENCE in an Indian setting is limited, even though there has been an extensive literature available in the western countries.

AIM OF THE STUDY

To Explore the relationship between Severity of alcohol dependence

a) Family History of Alcoholism.

b) Age of Onset of Alcohol use.

OBJECTIVES

1. To compare the SEVERITY OF ALCOHOL DEPENDENCE in two groups divided on the basis of presence or absence of family history of alcohol use in the first and second-degree relatives.
2. CORRELATE SEVERITY OF ALCOHOL DEPENDENCE WITH FAMILY HISTORY DENSITY IN SUBJECTS
3. To assess the AGE OF ONSET OF ALCOHOL USE and to correlate this with SEVERITY OF ALCOHOL DEPENDENCE.

MATERIALS & METHODS

A. SAMPLE/SETTING:

It was felt that we need to study a large enough population to address the major aims of the study. Patients admitted into the Institute of Mental Health, Chennai for alcohol related problems were to be enrolled into the study. The Hospital is a Psychiatry referral center for the urban and rural population of Chennai and neighboring states. There is an inpatient Alcohol Deaddiction treatment programme

Without knowledge of what proportion would be positive for family history a statistically derived sample size was not feasible. Sample size is set as 200 to ensure that we would have a good range with regard to the spread of age of onset of alcohol use. The Pts are recruited consecutively from the Deaddiction Clinic of Institute of mental Health for this study.

The inclusion criteria limited to male subjects because the numbers of female subjects found in the previous hospital records were very few and may not be statistically significant. Also, the age of these patients were between 20-50 because most of the patients getting admitted were in this group and only few were in the extremes of the age. The subjects who were medically too ill to cooperate for the interview or associated with major psychiatric illness such as psychosis, dementia, amnestic syndromes and bipolar affective disorder were excluded.

INCLUSION CRITERIA

1. Male subjects
2. Ages between 20 -50 years
3. Subjects with problem drinking in the past one year scoring more than 8 on AUDIT.
4. Informed consent for participation in the study.

EXCLUSION CRITERIA

1. Subjects associated with major psychiatric illness such as psychosis, dementia, amnestic syndromes and bipolar affective disorder.
2. Any independent physical illness where the subject is too ill to cooperate for the study.
3. History of other substance use (other than Tobacco) in the past year

MEASUREMENTS:

1. ALCOHOL USE DETECTION INVENTORY TEST (AUDIT)⁶⁵

AUDIT is a 10 item-screening questionnaire developed by W.H.O to identify persons whose alcohol consumption has become harmful to their health. It contains 3 questions on the amount and frequency of drinking, 3 questions on alcohol dependence and 4 on problems caused by alcohol. It takes 2 minutes to administer. It has a good test retest reliability, internal consistency and validity. Srinivasan & Mary and Sateesh Babu & Sen Gupta⁵⁹ have used AUDIT in Indian Context. Srinivasan & Mary Augustine⁶⁴ who used English versions of AUDIT, were able to detect 21% of subjects with harmful use of alcohol in there sample. Sateesh Babu & Sen Gupta⁵⁹ after screening there patients with MAST which detected 14.6 % to have problem drinking and the rest who were screened using the AUDIT did not qualify for problem drinking.

Prior to assessment for the study one had to ensure: –

1. That patient was not in alcohol withdrawal
2. That they were willing to participate in the study.
3. CIWA-AD was used to confirm that subjects were not in withdrawal.

2. CLINICAL INSTITUTE WITHDRAWAL ASSESSMENT FOR ALCOHOL (CIWA- AD)⁶⁶

It is 8-item scale for clinical quantification of the severity of the alcohol withdrawal syndrome. Its origin stems from the 15 items CIWA-A and the revised ten-item CIWA-AR (Sullivan et al, 1989). It is reliable, brief and clinically useful scale. A score of less than or equal to 8 indicates that the withdrawal symptoms have either subsided or very minimal. This scale offers increase inefficiency over the original CIWA-A scale, while retaining the clinical usefulness, validity and reliability. It takes 2-5 minutes to administer. Manikant et al⁶⁷ have used CIWA in the Indian context. They found that the CIWA-A score on the first day was 13.68 ± 2.37 (after 22 hrs of the last drink) which showed gradual reduction on the eighth day (1.68 ± 1.47) with benzodiazepine therapy.

3. SEVERITY OF ALCOHOL DEPENDENCE

Earlier studies have attempted to study severity of alcoholism in different ways. Some authors have used the quantity of alcohol, some have emphasized on the social consequences or health related problems as Severity of alcoholism. After Edwards & Gross⁶⁸ postulated the existence of common core of symptoms termed alcohol dependence syndrome, most of the studies started looking into the concept and started assessing and using measures based on this concept. Various scales to measure Severity

of alcohol dependence were subsequently was prepared. They include Rand Dependence scale, The Severity of Alcohol dependence questionnaire (SADQ), the severity of alcohol dependence data, the Last Month of Drinking Withdrawal scale and Last six Months of Drinking Impaired control and Dependence scale⁶⁹. Of these SADQ and SADD had a 59% agreement between them and significantly high correlation between them. SADD has been used in Indian context by John Abraham and Chandrasekaran. Scale like SADQ even though not used in Indian context it is easy and simple to use and of relevance in a clinical context. This questionnaire was developed to provide a brief and replicable method of assessing alcohol dependence. It is a 20-item self-completion questionnaire in which the respondents are required to focus upon a recent month typical of their heavy drinking. There are four items in each of the five sections used. They include:

1. Physical withdrawal signs
2. Affective withdrawal signs
3. Withdrawal relief drinking
4. Quantity & frequency of alcohol consumption
5. Rapidity of reinstatement of withdrawal symptoms following a period of abstinence.

Each item is rated upon a four-point scale (Almost never, Sometimes, often and nearly always) and responses are scored as 0, 1, 2 or 3 accordingly. Thus, the range of total score is from 0-60. A score of 31 or higher is correlated with severe alcohol dependence and less than 30 is correlated with mild to moderate dependence. It takes around five minutes to complete the instrument. It has a very high degree of test and retest reliability and a very good evidence of construct and concurrent validity.

4. FAMILY HISTORY METHOD

Family History of Alcoholism has proved to be of one of the important risk factor in the development of alcoholism. It is viewed as an index of “biopsychosocial” risk since it encompasses “a rich medley of intertwined vulnerability factors”. In various studies, individuals with a positive family history have shown to have an earlier age of onset, to have a severe illness, a worse prognosis, dissocial personality disorder and vocational, social and physical complications. Also alcoholics with one or both parents alcoholic show more severe course of alcoholism⁷¹.

In this method the subjects are divided into family history positive and negative groups. Unfortunately, there are no standard family history methods, which are generally accepted as the standard method, (Turner et al⁴⁰ 1993). Cotton⁷² has examined 27 studies involving positive familial

alcoholism, it revealed that all authors accepted paternal alcoholism as evidence of a positive history, 21(78%) accepted maternal or paternal alcoholism, 2(7%) also accepted grandparental alcoholism and 20(74%) accepted alcoholism among siblings. Schuckit and Smith⁷³ on the basis of Father's alcoholism divided the families into Family History Positive (FHP) and negative (FHN). Parental alcoholism has also been used in many studies to differentiate Family History of Alcoholism. Some authors have used first-degree measure to differentiate Family History of Alcoholism; Family History Positive is defined as having any first degree relative (biological parents or sibling) with alcoholism. Father, Parent and First-degree measures are dichotomous measures.

In an attempt to improve and standardize the classification Alterman⁷⁴ made attempts to compare the four types of Family History of Alcoholism Classification, they included, (1) Conventional methods-involving only first or second degree relatives, (2) Lineal method-involving alcoholism in parents or grandparents but distinguishing between paternal and maternal lineage, (3) generational method – alcoholism occurring in the paternal or grandparental generations and (4) quantitative method – which is an operationalized weighted scoring method, where one point is added for each first degree alcoholic relative (parent or sibling) and half a point is added for each second degree alcoholic relative

(grandparent or uncle). Alterman found few differences using the quantitative method and noted the limitations of using the dichotomous classifications. But the pitfall in his study was that there were relatively small sample sizes ($n=83$), and they were further divided into 3 subcategories.

In 1993, Turner introduced a new quantitative method of classification called Family Pattern of Alcoholism (FPA). In this method, the subject indicated the drinking history of each family member by constructing a family tree. It is mentioned that each family member were assessed and were rated as an abstainer, problem drinker or non-problem drinker but it is not clearly mentioned whether they were assessed directly or indirectly with informants. The parents and the grandparents were given a score of 1 if they were found to be a problem drinker and a score of 0 if they were found to be an abstainer or a non-problem drinker. In order to control for number of aunts, uncles and siblings for each category, the proportion of problem drinkers to the total membership in the category was calculated. In the end, the sum of all the scores of the reported relatives were taken and analysed. Turner compared FPA method to other methods of and found that FPA explained more variance in the Age of Onset, Severity and consequence of drinking in male inpatients. This study suggested the value of moving from older methods of measure to a

standard and quantitative method which is more amenable for more sophisticated statistical analysis (Turner et al, 1993)

Scott.F.Stoltenberg⁷⁵ proposed a new FH measure called the Family History Density (FHD), which is a modification of FPA. In this method, weighted points were given to the alcoholic family members (both parents and all four grandparents). The non-alcoholic relatives were given a score of zero, parents were given a score of 0.5 and grand parents were given 0.25. The scores were summed over the six ancestors to obtain the FHD score, which ranged from 0-2. FHD differed from FPA into two ways. First, it uses information from both parents and grandparents, who are the direct ancestors of the proband whereas FPA uses information from aunts, uncles and siblings. FPA uses arbitrary dummy codes. Information about the aunts, uncles and siblings were excluded. Since the FHD is a measure of “biopsychosocial” risk. Grandparents cannot be interchanged for aunts and uncles because the former have a greater potential influence and maintain the rearing conditions of the parents, aunts and uncles. Therefore the grandparents have a more direct path of influence than do aunts and uncles. The scoring system is based on the familial relatedness, which is functionally same as genetic relatedness and theoretically explicit because it takes into account the influence of family environment (parents are expected to influence the proband directly than the grandparents). Mothers

were also included in this scoring system since FHD is an index of biopsychosocial measure, which includes the deleterious effects of drinking during pregnancy, and not limited to fetal alcohol syndrome. One limitation of the study was that study involves the use of self reports accounts to measure the family History of Alcoholism, however Gershon and Guroff⁷⁶ have shown that self reports of FH of alcoholism is less biased and reliable when compared with FH diagnosis of other psychiatric disorders.

In the same study other FH measures were compared with FHD and found that all the FH measure were associated with alcohol dependence diagnosis, development of tolerance and experiencing withdrawal symptoms in men where as in women FHD and Parent measures were significantly associated with all three outcomes⁴⁰.

Information from the relatives about the six direct ancestors was assessed by using Family Interview for Genetic Studies⁷⁷ (FIGS), which is based on Research Diagnostic Criteria FIGS is a guide for gathering information about relatives in the pedigree to be studied. It is particularly important when the information from the subject is not reliable. It is meant to be a guide for the interviewer and enables freedom in wording the questions. We used the alcohol section of FIGS to collect alcohol history from the relatives of the proband. The density of family history was

quantified using the method described by Zucker et al⁷⁹. In this method, weighted points were given to the alcoholic family members (both parents and all four grandparents). The non-alcoholic relatives were given a score of zero, parents were given a score of 0.5 and grand parents were given 0.25. The scores were summed over the six ancestors to obtain the FHD score, which ranged from 0-2.⁷⁸

We have considered both the conventional dichotomy method and the Family History Density Method. These methods were chosen in order to compare and contrast the methodological issues. The dimensional measure would also enable co-relational analysis with other variables of interest.

5. AGE OF ONSET OF PROBLEM DRINKING (AOO)

The AGE OF ONSET OF PROBLEM DRINKING and later development of alcohol related problems and dependence is well established in the cross-sectional as well as longitudinal studies. There are basically two types of alcoholics called as EARLY ONSET ALCOHOLICS and LATE ONSET ALCOHOLICS, which have been described, in the earlier paragraphs. A potentially powerful predictor of progression to alcohol-related harm is age at first use. Evidence suggests that the earlier the age at which young people take their first drink of alcohol, the greater the risk of abusive consumption and the development

of serious problems, including alcohol disorders. In many societies the use of alcohol during the teenage and young adult years is a common phenomenon. For large numbers of youth it may signify nothing more than healthy psychological experimentation⁷⁹. It is also true that many drinkers reduce their consumption in early adulthood to conform to the expectations and obligations of adult social roles such as marriage, childbearing, and employment (the role-incompatibility theory)⁸⁰. However, epidemiological data have shown that a substantial minority of lifetime alcohol users (20%-50%) progress to one or more alcohol problems or become alcohol dependent.⁸¹ The concept of “AGE OF ONSET” has been a phenomenological advance and the look out for a perfect definition is still a controversy. Most of the authors have a different consensus about the AGE OF ONSET of alcoholism. Lee and Diclemente defined AOO as “the age at which a consistent pattern of heavy alcohol use was established” and “the duration of problem drinking”, Irwin, Schuckit & Smith studied defined AOO as “age at which subject first met the DSM3R criteria for Alcohol abuse or dependence” and Grant et al defined AOO “age at which they first started drinking, not counting small tastes or sips of alcohol”.⁵⁰ But most of the studies have consistently shown that the age of onset of problem drinking has shown to lead to dependence and is the actual measure of AOO. Our operational definition was “The age in which drinking first began to have an effect on the subjects life of which he or she

did not approve” (Johnson et al³², 2000). We assessed the Age of onset from the alcohol section of SCAN.

6. SCHEDULE FOR CLINICAL ASSESSMENT IN NEUROPSYCHIATRY⁸² (SCAN)

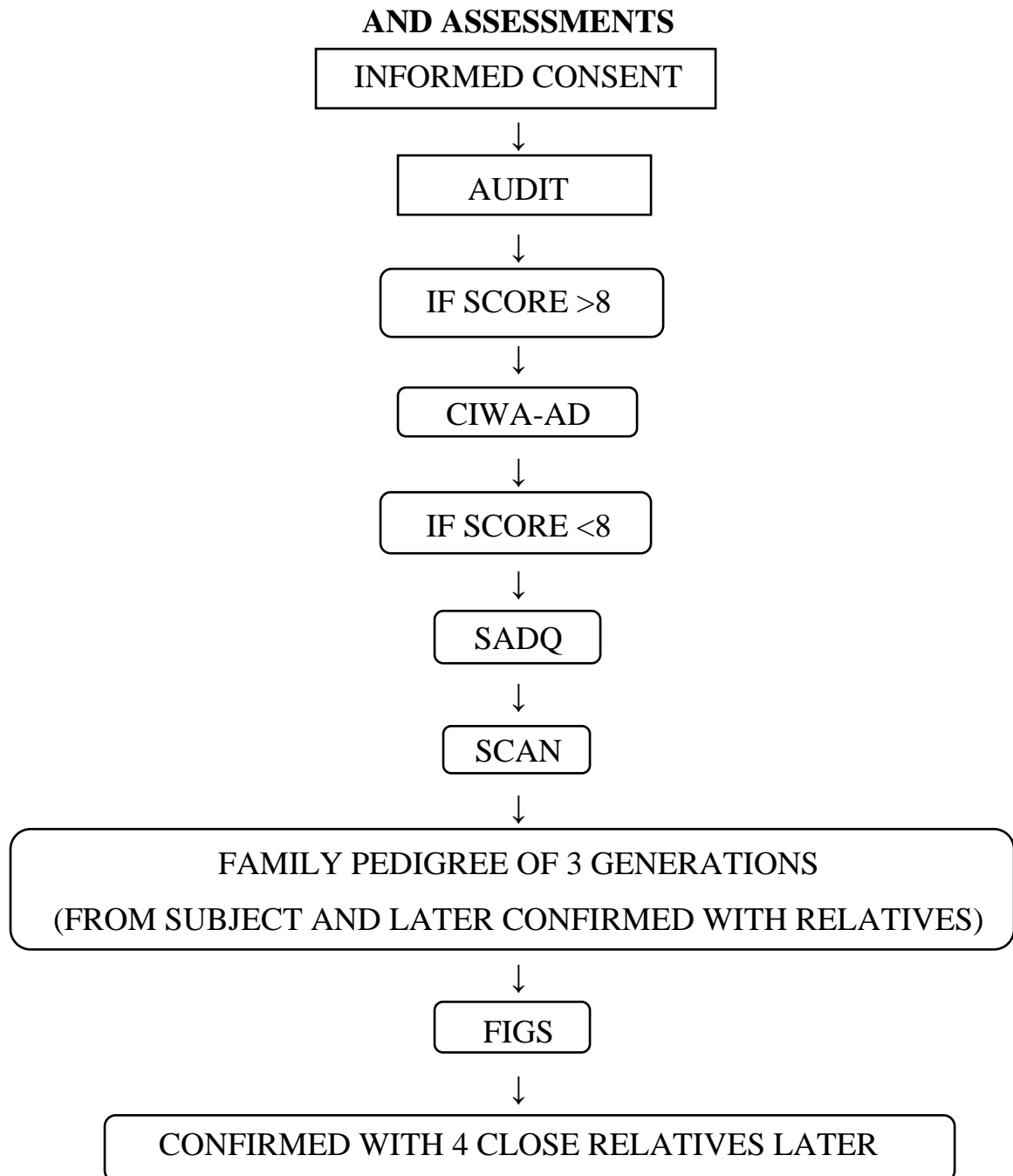
SCAN is a set of instrument aimed at assessing, measuring and classifying psychopathology and syndromal diagnosis. The current version is 2.1. Alcohol section was used to get the age of onset of harmful use and to establish a diagnosis of Alcohol dependence syndrome based on the 10th edition of International classification of diseases and screening section of this assessment was used to rule out any major psychiatric illness such as psychosis, bipolar affective disorder, dementia and amnestic syndromes

STATISTICAL ANALYSIS

The data was analysed using a computerized Statistical Software programme (SPSS version 20.0 for windows). Descriptive statistics was used to describe the socio-demographic variables. Student t-test was used to compare between ordinal groups. Pearson’s correlation was used for assessing the correlation between the variables.

FIGURE. 1.

FLOW CHART SHOWING THE PROCESS OF SCREENING



RESULTS

The planned samples of 200 subjects for the study were obtained from the patients who came for consultation to the hospital over a 6 months period. Patients refused participation, patients with poor details of the relative, patients who had AUDIT score of less than 8 and did not qualify for the inclusion criteria. Patients with medical complications were excluded.

TABLE.4. SHOWING THE CURRENT AGE OF ONSET AND SOCIOECONOMIC PARAMETERS AND OTHER VARIABLES

Current age	20-25	26-30	31-35	36-40	41-45	46-50	Total	Mean	SD
AOO <25	9 (4.5%)	18 (9%)	21 (10.5%)	20 (10%)	20 (10%)	28 (14%)	116 (58%)	19.33	6.12
AOO >25	0	6 (3%)	11 (5.5%)	15 (7.5%)	19 (9.5%)	33 (16.5%)	84 (42%)	14	11.45

FHP	8 (4%)	21 (10.5%)	22 (11%)	17 (8.5%)	23 (11.5%)	32 (16%)	123 (68.5%)	20.5	7.87
FHN	1 (0.5%)	3 (1.5%)	10 (5%)	18 (9%)	16 (8%)	29 (14.5%)	77 (13.5%)	12.83	10.42
FHD 0 Group1	1 (0.5%)	3 (1.5%)	10 (5%)	18 (9%)	16 (8%)	29 (14.5%)	77 (38.5%)	12.83	10.42
0.25-0.5 Group2	5 (2.5%)	11 (5.5%)	13 (6.5%)	11 (5.5%)	14 (7%)	16 (8%)	70 (35%)	11.67	3.78
0.75-2 Group3	3 (1.5%)	10 (5%)	9 (4.5%)	6 (3%)	9 (4.5%)	16 (8%)	53 (26.5%)	8.83	4.36

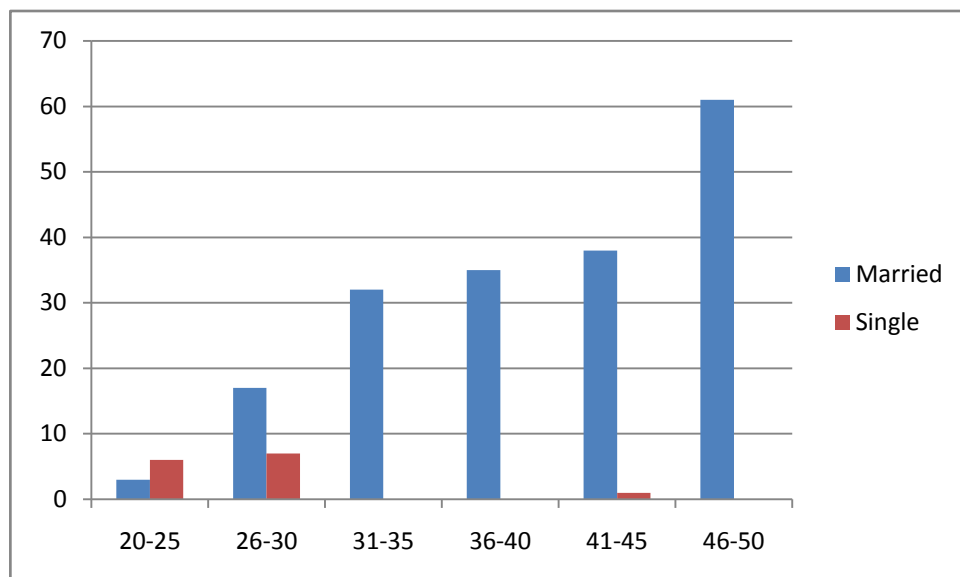
Severity Mid- mod	1 (0.5%)	2 (1%)	3 (1.5%)	5 (2.5%)	2 (1%)	7 (3.5%)	20 (10%)	3.33	2.25
Severe	8 (4%)	22 (11%)	29 (14.5%)	30 (15%)	37 (18.5%)	54 (27%)	180 (90%)	30	15.32
Income <1000	2 (1%)	5 (2.5 %)	4 (2%)	2 (1%)	2 (1%)	5 (2.5%)	20 (10%)	19.5	8.38
1001- 5000	6 (3%)	15 (7.5%)	21 (10.6%)	27 (13.6%)	19 9.5%)	29 (14.6%)	117 (58.8	19.5	8.38
5001- 10000	0	2 (1%)	5 (2.5%)	2 (1%)	13 (6.5%)	17 (8.5%)	39 (19.6%)	6.5	6.89
>10001	1 (0.5%)	2 (1%)	1 (0.5%)	4 (2%)	5 (2.5%)	10 (5%)	23 (11.6%)	3.83	3.43
SD=STANDARD DEVIATION, AOO=AGE OF ONSET; FHP=FAMILY HISTORY POSITIVE, FHN=FAMILY HISTORY NEGATIVE.									

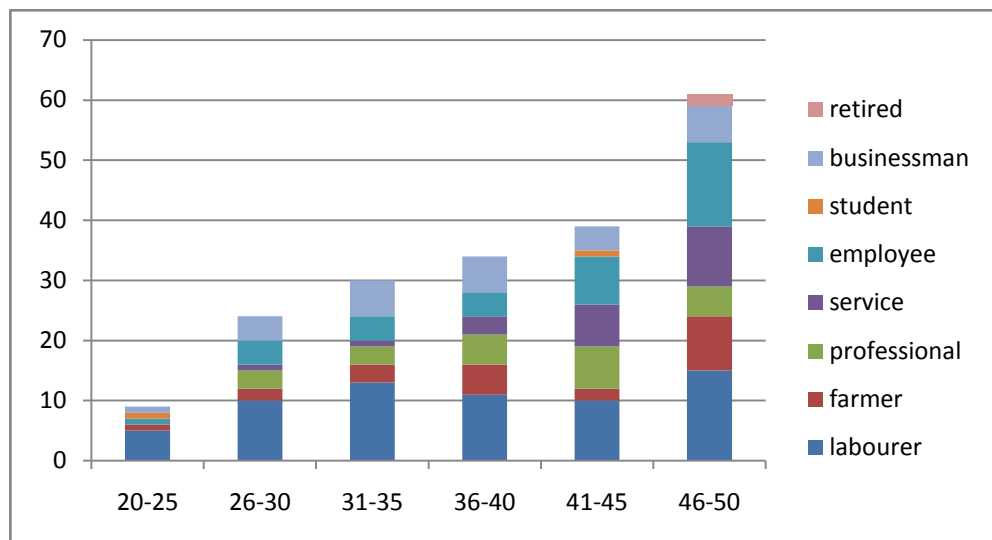
Current age	20-25	26-30	31-35	36-40	41-45	46-50	Total	Me an	SD
Married	3 (1.5%)	17 (8.5%)	32 (16%)	35 (17.5%)	38 (19%)	61 (30.5%)	186 (93%)	31	19.73
Single	6 (3%)	7 (3.5%)	0	0	1 (0.5%)	0	14 (7%)	2.33	3.27
Joint	1 (0.5%)	2 (1%)	3 (1.5%)	1 (0.5%)	0	3 (1.5%)	10 (5%)	1.67	1.21
Extended	1 (0.5%)	4 (2%)	4 (2%)	1 (0.5%)	1 (0.5%)	3 (1.5%)	14 (7%)	2.33	1.51
Alone	0	1 (0.5%)	0	0	0	0	1 (0.5%)	0.17	0.41
Nuclear	7 (3.5%)	17 (8.5%)	25 (12.5 %)	33 (16.5%)	38 (19%)	55 (27.5%)	175 (87.5)	29.1 7	16.83

Occupation Laborer	5 (2.5%)	10 (5%)	13 (6.5%)	11 (5.5%)	10 (5%)	15 (7.5%)	64 (32%)	10.6 7	3.39
Farmer	1 (0.5%)	2 (1%)	3 (1.5%)	5 (2.5%)	2 (1%)	9 (4.5%)	22 (11%)	3.67	2.94
Professionals	0	3 (1.5%)	3 (1.5%)	5 (2.5%)	7 (3.5%)	5 (2.5%)	23 (11.5%)	3.83	2.40
Service	0	1 (0.5%)	1 (0.5%)	3 (1.5%)	7 (3.5%)	10 (5%)	22 (11%)	3.67	3.98
Employee	1 (0.5%)	4 (2%)	4 (2%)	4 (2%)	8 (4%)	14 (7%)	35 (17%)	5.83	4.58
Student	1 (0.5%)	0	0	0	1 (0.5%)	0	2 (1%)	1.33	2.34
Businessmen	1 (0.5%)	4 (2%)	6 (3%)	6 (3%)	4 (2%)	6 (3%)	27 (13.5	4.5	1.97
Retired	0	0	0	0	0	2(1%)	2(1%)	0.33	0.82

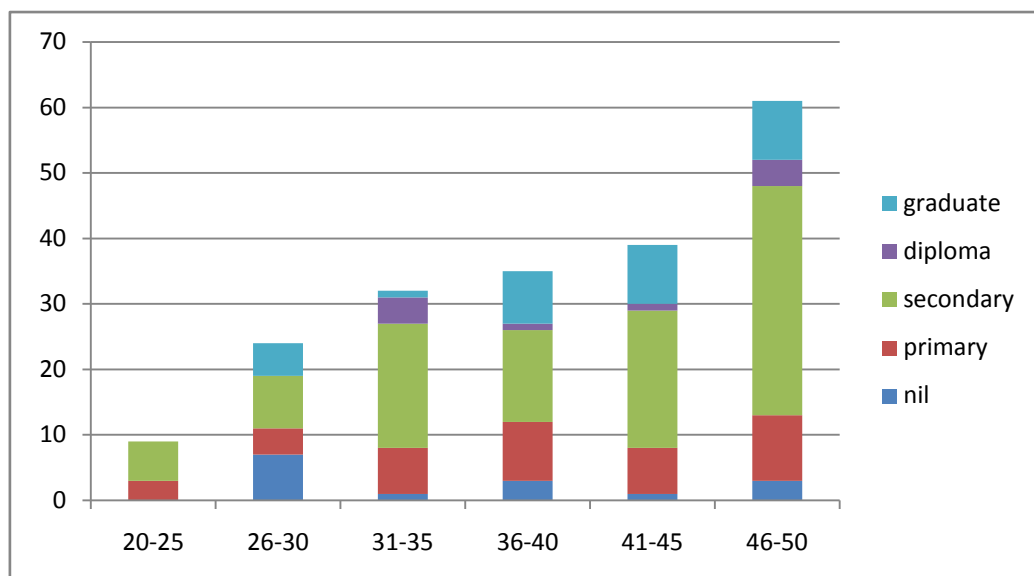
Education Primary	3 (1.5%)	4 (2%)	7 (3.5%)	9 (4.5%)	7 (3.5%)	10 (5%)	40 (20%)	6.67	2.73
Secondary	6 (3%)	8 (4%)	19 (9.5%)	14 (7%)	21 (10.5%)	35 (17.5%)	103 (51.5%)	17.7 0	10.53
Graduate	0	5 (2.5%)	1 (0.5%)	8 (4%)	9 (4.5%)	9 (4.5%)	32 (16%)	3.33	4.03
Diploma	0	0	4 (2%)	1 (0.5%)	1 (0.5%)	4 (2%)	10 (5%)	1.67	1.86
No Education	0	7 (3.5%)	1 (0.5%)	3 (1.5%)	1 (0.5%)	3 (1.5%)	15 (7.5%)	2.30	2.51

As shown in the figure above, 200 male subjects scoring more than 8 on the AUDIT were recruited in the study over a period of 6 months. Their current ages ranged from 20-55 yrs. As shown in table (4) 123 subjects were FAMILY HISTORY POSITIVE and 77 were FAMILY HISTORY NEGATIVE. In the FHP group, 8 (4%) were in the 20-25 yrs of current age, 21(10.5%) were in the 26-30 age group, 22(11%) were in the 31-35 age group, 17(8.5%) were in the 36-40 age group,





23(11.5%) were in the 41-46 age group and 32(16%) were in the 46-50 group. In the FHN group, 1 (0.5%) were in the 20-25 yrs of current age, 3(1.5%) were in the 26-30 age group, 10(5%) were in the 31-35 age group, 18(9%) were in the 36-40 age group, 16(8%) were in the 41-45 age group and 29(14.5%) were in the 46-50 age group.



FAMILY HISTORY DENSITY consisted of three groups; they included Group1 where the total FH score was 0, Group 2 where the FH

score was between 0.25-0.5 and group 3 where the score was 0.75-2. The FHD 0 group had 77 subjects, 0.25-0.5 had 70 subjects and 0.75-2 group had 53 subjects. In the Group2, 5 (2.5%) were present in the 20-25 yrs of current age, 11(5.5%) were in the 26-30 age group, 13(6.5%) were in the 31-35 age group, 11(5.5%) were in the 36-40 age group, 14(7%) were in the 41-46 age group and 16(8%) were in the 46-50 group. In the Group3, 3(1.5%) were present in the 20-25 yrs of current age, 10(5%) were in the 26-30 age group, 9(4.5%) were in the 31-35 age group, 6(3%) were in the 36-40 age group, 9(4.5%) were in the 41-46 age group and 16(8%) were in the 46-50 group.

In the Family History Density scoring all the 6 direct ancestors were taken into analysis and other family members were excluded. They included Father, Mother, Paternal Grandfather, Paternal Grand mother, Maternal Grand father and Maternal Grand mother. The Table 6 shows the status of Family members positive and Negative in the each FHD group.

TABLE.5 SHOWING THE STATUS OF FAMILY MEMBERS IN THE FHD GROUPS.

FHD	STATUS	GROUP 1	GROUP 2	GROUP 3	TOTAL
FATHER	Positive	0	55(27.5%)	53(26.5%)	108(54%)
	Negative	77(38.5%)	15(7.5%)	0	92(46)
MOTHER	Positive	0	0	10(5	10(5
	Negative	77(38.5%)	70(35%)	43(21.5%)	190(95%)
Paternal Grand Father	Positive	0	10(5 %)	42(21%)	52(26%)
	Negative	77(38.5%)	60(30%)	11(5.5%)	148(74%)
Paternal Grand Mother	Positive	0	0	6(3%)	6(3%)
	Negative	77(38.5%)	70 35%)	47(23.5%)	194(97%)
Maternal Grand Father	Positive	0	8 (4%)	30 (15%)	38(19%)
	Negative	77(38.5%)	62 (31%)	23(11.5%)	162 (81%)
Maternal Grand Mother	Positive	0	0	9 (4.5%)	9 (4.5%)
	Negative	77(38.5%)	70 (35%)	44 (22%)	191(95.5 %)
FHD=FAMILY HISTORY DENSITY; GROUP1=FHD SCORE OF ZERO; GROUP2=FHD SCORE BETWEEN 0.25-0.5; GROUP3=FHD SCORE BETWEEN 0.75-2					

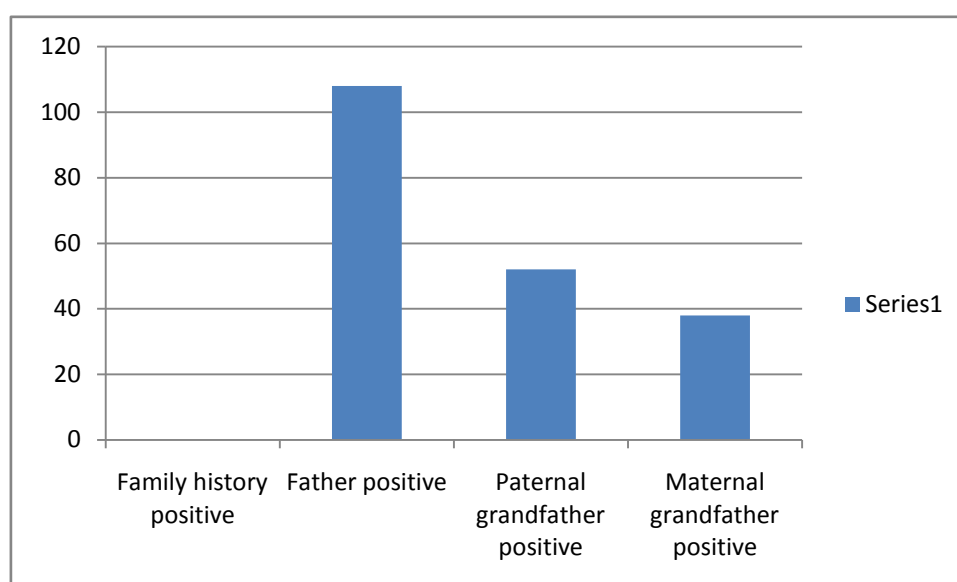
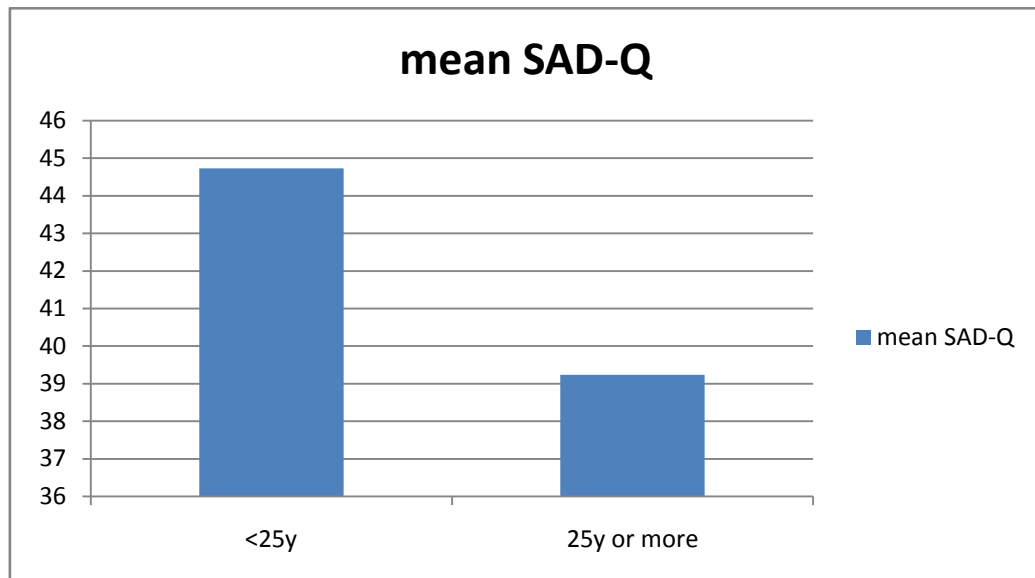


TABLE.6. COMPARING THE AGE OF ONSET WITH CURRENT AGE AND SADQ SCORES					
<u>AGE OF ONSET</u>	NO	MEAN CURRENT AGE	S	MEAN SADQ	S
<25yrs	116	38.08 (SD=8.56)	p=0.00 0	44.73 (SD=10.66)	p=0.00 1
>OR EQUAL TO 25	84	42.56 (SD=6.76)		39.24 (SD=11.6 3)	
S=significance.					

The AGE OF ONSET was divided into two groups. First group consisted of AOO <25yrs and the second group was AOO >25yrs. It can be seen from the TABLE. 6 that the mean severity scores were significantly different between the EAOO and LAOO groups. In the first group, 9(4.5%) were present in the 20-25 yrs of current age, 18(9%) were in the 26-30 age group, 21(10.5%) were in the 31-35 age group, 20(10%) were in the 36-40 age group, 20(10%) were in the 41-46 age group and 28(14%) were in the 46-50 group. In the second group, there were none in the 20-25 yrs of current age, 6(3%) were in the 26-30 age group, 11(5.5%) were in the 31-35 age group, 15(7.5%) were in the 36-40 age group, 19(9.5%) were in the 41-46 age group and 33(16.5%) were in the 46-50 group.



The Severity of alcohol dependence as assessed by SADQ, was divided into two groups based on a cut off point at 30. The first group with a score of less than 30 belonged to the Mild-Moderate group and the second group with a score of more than 30 belonged to the severe group. In the mild to moderate group, 1 (0.5%) 20-25 yrs of current age, 2(1%) were in the 26-30 age group, 3(1.5%) were in the 31-35 age group, 5(2.5%) were in the 36-40 age group, 2(1%) were in the 41-46 age group and 7(3.5%) were in the 46-50 group. In the Severe group, 8(4%) 20-25 yrs of current age, 22(11%) were in the 26-30 age group, 29(14.5%) were in the 31-35 age group, 30(15%) were in the 36-40 age group, 37(18.5%) were in the 41-46 age group and 54(27.5%) were in the 46-50 group.

**TABLE. 7. COMPARING FAMILY HISTORY
(DICHOTOMY) WITH CURRENT AGE, AGE OF
ONSET AND SADQ SCORES**

FAMILY HISTORY	NO	MEAN CURRENT AGE	MEAN AGE OF ONSET	S	MEAN SADQ	S
POSITIVE	123	38.61 (SD=8.59) NS	22.89 (SD=4.61)	P=0.000	44.59 (SD=10.79)	P=0.001
NEGATIVE	77	42.12 (SD=6.90)	26.51 (SD=5.90)		38.96 (SD=11.50)	
S= Significance; NS - Non significant						

The above shows the association of FH (Dichotomy) with Current age, Mean AOO and Mean SADQ score. The mean Current Age in the FHP was 38.61 ± 8.59 and 42.12 ± 6.90 in FHN. The Mean AOO in the FHP was 22.89 ± 4.61 and in the FHN was 26.51 ± 26.51 and was significantly different from each other. ($P>0.000$) The Mean SADQ score were 44.59 ± 10.79 in FHP and 38.96 ± 11.50 in the FHN. This was also significantly different between the two groups ($P>0.001$).

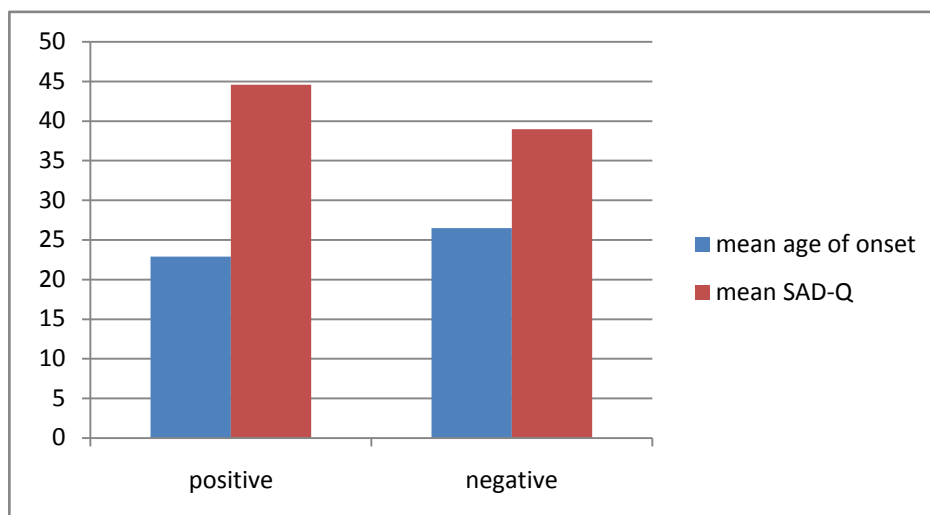


TABLE. 8.
SHOWING THE CORRELATION OF SEVERITY
WITH OTHER VARIABLES STUDIED

Factor Studied	Variables Studied	Pearson's Correlation	Significance
Severity	Current age	-0.075	not significant
Severity	Family history density	-0.287	p=0.01
Severity	Age of onset	-0.346	p=0.01
PARTIAL CORRELATION BETWEEN SEVERITY AND FHD, AFTER CONTROLLING FOR AGE OF ONSET INCREASED FROM p=0.01 TO p=0.000. HOWEVER THE PARTIAL CORRELATION BETWEEN, SEVERITY AND AOO AFTER CONTROLLING FOR FHD WAS THE SAME.			

The above table shows the correlation between FHD, Current Age, AOO and Severity. The mean current age in the group1 was 42.2 ± 6.90 , group2 was 38.53 ± 8.44 and 38.72 ± 8.86 in the last group. The correlation was not statistically significant. The mean AOO was in the group1 was 26.51 ± 5.90 , group2 was 23.29 ± 5.11 yrs and 22.36 ± 3.83 yrs in the last group. The correlation between FHD and Mean AOO were statistically significant (p=0.001). The mean SADQ in the group1 was 38.9 ± 11.50 , group2 was 43.43 ± 10.78 and 46.13 ± 10.71 in the last group. The relationship between FHD and the mean SADQ scores were also significant (p=0.01). On analyzing the partial correlations, the significance of FHD with SEVERITY increased from p=0.01 to p=0.000 (coefficient of

–0.2931 and df =197), after controlling for AOO and the significance value of AOO and Severity remained the same after controlling for FHD.

TABLE.9
TABLE SHOWING THE RELATIONSHIP BETWEEN
FHD AND SUBSCORES OF SADQ SCALE

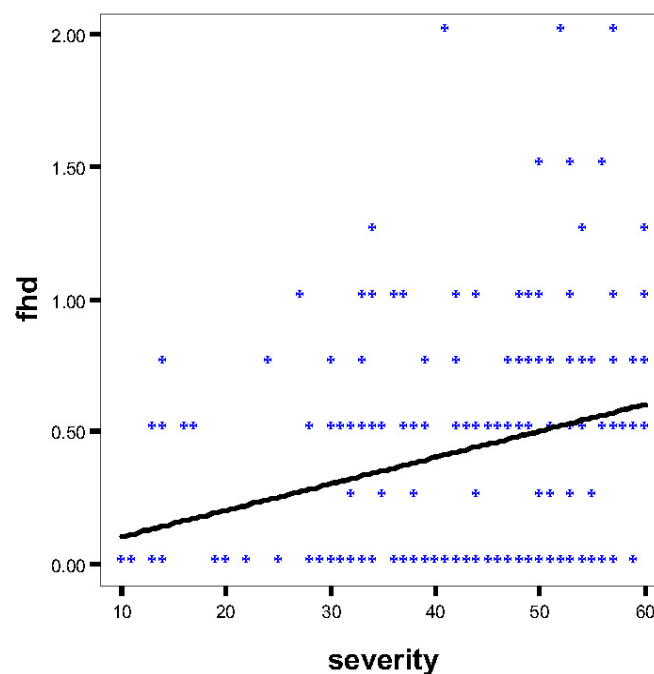
	FHDSCALE	SGRP 1	SGRP 2	SGRP 3	SGRP 4	SGRP 5
FHDSCALE Pearson Correlation Sig. (1-tailed) N	1.000	.224**	.157*	.116	.116	.193**
SGRP1 Pearson Correlation Sig. (1-tailed) N	.224**	1.000	.373**	.280**	.246**	.513**
SGRP2 Pearson Correlation Sig. (1-tailed) N	.157*	.373**	1.000	.206**	.252**	.379**
SGRP3 Pearson Correlation Sig. (1-tailed) N	.116	.280**	.206**	1.000	.314**	.605**
SGRP4 Pearson Correlation Sig. (1-tailed) N	.116	.246**	.252**	.314**	1.000	.332**
SGRP5 Pearson Correlation Sig. (1-tailed) N	.193**	.513**	.379**	.605**	.332**	1.000

* Correlation significant at p value < 0.05

* Correlation significant at p value < 0.01

The above table 9 shows significant correlation of FHD with subgroup 1, 2 and 5 of SADQ values. They include Physical withdrawal signs ($p=0.01$), Affective withdrawal signs (0.05) and Rapidity of reinstatement of withdrawal symptoms following a period of abstinence (0.01). The Withdrawal relief drinking and Quantity & frequency of alcohol consumption did not correlate with FHD.

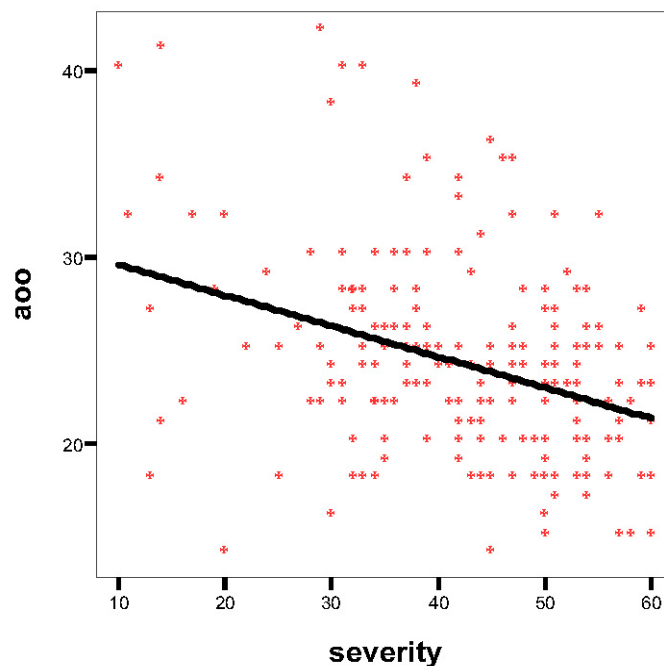
FIGURE-2
GRAPH SHOWING THE RELATIONSHIP
BETWEEN FHD AND SEVERITY



FHD=FAMILY HISTORY DENSITY SCORES

The graph shows the relationship between the severity and Family History Density. As the FHD score increases the severity also increases.

FIGURE-3
GRAPH SHOWING THE RELATIONSHIP
BETWEEN AOO AND SEVERITY



AOO=AGE OF ONSET

This graph shows the relationship between Severity and Age Onset. From the graph we may infer that, as the Age of Onset is early the severity also increases.

Discussion

We have studied 200 subjects with problem drinking who had sought help in Institute of Mental Health. We have evaluated them for Severity of Alcohol Dependence, Age of Onset of alcohol use and rigorously looked at the Family History of alcoholism.

The results section highlights the following:

1. Severity of alcohol dependence is significantly different in presence of Positive family history of Alcoholism (table 7)
2. Family history density is significantly correlated with Severity of Alcohol dependence in the index subjects (table 8)
3. Age of onset of alcohol use is significantly correlated with Severity of Alcohol dependence in the subjects. (Table 6)

The above findings answer the three main aims of the study. In addition we found that Sub-scales of severity are all significantly related to family history density. This is particularly important for the sub scales on physical withdrawal signs and rapidity of reinstatement after abstinence. We will now discuss the above findings under the following headings:

1. Setting / Sample
2. Measures of severity, family history and age of onset
3. Implications of the study
4. Limitations
5. Future directions

1. Setting/Sample:

This study was conducted in Institute of mental health where alcoholic patients of varied severity seek help for different alcohol related health problems. In our subjects, minimum SADQ score was 10 and the maximum was 60, with a mean of 42.43 (± 11.38). Although our original plan was to target a widely ranged sample from a severity point of view by using subjects of varied severity, since most of the patients are admitted in De-addiction ward and hence this understandably has skewed the sample towards higher range of severity. We have seen only problem drinkers as per AUDIT criteria. There may be others in the community who may score less on AUDIT but have frequent use of alcohol. Therefore this is a study of severity of alcohol dependence in a group of AUDIT defined subjects with harmful use and not a study of all alcohol use. However, different thresholds for screening may be attempted in the community samples so that a wider spectrum of severity can be obtained. Alternatively a study

looking at a large sample with stratified levels of severity can be an improvement on this design. The patients were screened using stringent criteria by AUDIT to look for problem or hazardous drinking.

Screening criteria: One could argue that the items in AUDIT which leads to the score of 8 and identifies problem drinkers may be more likely to identify severe end of spectrum of 'heavy alcohol use'. Whether use of different severity cut-off could still identify enough subjects with 'problem drinking' who could be representatives of samples needed for meeting our aims/objectives is something to be considered.

Medical illness/consent issues

A study focussed on correlates of severity of alcohol use, a sample with a wider range of severity would increase confidence limits with regard to correlational analysis. Future studies need to focus on all these issues namely – screening criteria/populations, which can contribute a less severe sample than obtained from psychiatric wards. A community study with less stringent screening criteria would be definitely useful. Alternatively, stratified sampling covering a range of severity thresholds could be attempted from medical/surgical populations. Such a design would call for less rigid time constraints than could be afforded by this study.

We also have made sure that the subject is not in the withdrawal period as this can interfere in the assessment of various measures. Even though we have not blinded this study, the sequence of administration of the SADQ before interviewing the FH itself acted as a “blinding process”.

2. Measures of severity, family history and age of onset

1. SADQ. This is a self-report measure. This has not been standardised in an Indian context. In fact no measure standardised in an Indian context looking at Severity of alcohol use exists. As mentioned in the Section on Methods we chose this scale because it is easy and simple to use. The psychometric properties apply when it is used as a self-report measure. Its psychometric property when used, as an Interviewer scored method is not known. It is possible that some questions may be answered differently if it is scored as a self-report. This remains a limitation of the method. In fact Doherty & Webb ⁸³ has used this scale as an Interview format and felt that interview method prevents questions being misinterpreted. Also a related measure SADD (Severity of Alcohol Dependence Data) has been used in a community sample in the Indian context in an Interview based manner, although even this was meant to be used as a self-report measure. This highlights a major difficulty of Psychiatric research in India – namely lack of standardised measures for

use in local languages with demonstrable psychometric advantages. This is particularly so for self report measures. We however chose SADQ as it has been used in western studies looking at severity and its correlates as mentioned in the review of literature (Corrigan³⁵ et al 1986, Schachter²⁷ et al 1990, Keenan³⁰ et al 1996).

Then SADQ was administered on one to one interview basis to clarify doubts and to prevent any questions being misinterpreted. This scale has been used in mostly western studies. It has been correlated with Severity of Alcohol Dependence Data (SADD) and has 59% agreement with SADQ⁸³. SADD has been used in a one to one interview format in Indian studies (John Abraham & Chandrasekaran⁵⁸, 1997). The SADQ has not been available in the local languages and has not been validated in the Indian context. So a fixed list of translated questions is used as the initial probe. However validation or test-retest reliability of the translation was not done due to practical constraints. Some of the other measure for severity includes Addiction Severity Index, Alcohol Use Inventory. While comprehensive, it takes one hour to administer, which is one of the limiting factor especially in a study where many other measures are used.

2. Family history assessment method: This is a major strength of the study. FIGS is a well established tool in family research studies (Keenan³⁰ et al). It has been used in the Indian context¹⁵, We have managed to

interview on an average three additional family members apart from the index subject to obtain the information about all identified/indicated family members. We have used a categorical dimension (family history positive/negative) and also a dimensional measure (family history density). We believe that this method significantly improves reliability of the information, although may be less ideal than Individual subject face to face interview (Assanangkornchai S, et al³³). There has been no consensus on various definitions in the previous studies. In our study we have used both the recent measure of FH called Family History Density, which looks into FH as a “biopsychosocial index” rather than looking at the conflict of Genetic vs. Environment factors.

3. Age of Onset: Age of onset may be currently viewed as a continuum of disease with greater alcohol severity and associated psychopathology. Of all the variables impulsivity and Family History have been consistently shown to be associated with early age of onset as the comorbidity (Lewis & Bucholz³⁹, Jellinek¹⁸).

The interview was semi-structured and used information from all sources, including the many relatives of the index subjects who were contacted for the FIGS interview. SCAN has been field tested in India (WHO 1994) and the items especially leading to information about Age of onset of alcohol use are very simple and easy to administer and closely

mimic usual clinical interview. While this may not be a substitute for longitudinally derived information, we feel the information on this account can be considered reliable.

While Latcham³⁶ 1985 and Dejong and Roy²⁹ 1997 both used unstructured interviews, Worobec²⁶ 1990 obtained this information from user-lead questionnaires. Penick²⁵ et al 1987 obtained this from a structured Interview. It has been mentioned that Age of Onset is a phenomenological advance but without a perfect definition (Anderson⁵² et al) . A structured interview improves reliability especially when information is collected from a variety of sources.

3. Comparison with other studies:

The two key findings of this study are that alcoholism severity is related to family history of alcoholism and also age of onset of alcoholism independent of each other. The relationship with severity with positive family history of alcoholism is in agreement with many studies namely, Schuckit⁷¹ 1984, Worobec²⁶ 1990, Hauser and Rybakowski⁴³ 1997 and Assanangkornchai³³ 2002. This relationship holds good despite varying settings, samples and a variety of assessment methods. As mentioned earlier, Schachter²⁷ 1990 and Keenan³⁰ 1996 had different results. Schachter²⁷ et al did have a trend in the direction of greater severity in presence of positive family history. Their samples were derived from those

arrested for public drunkenness. Keenan³⁰ et al's study had only 36 subjects and may not have been powered to address this issue adequately. Of the Indian studies, one finds some indirect support for the association between positive family history and Severity of alcoholism from John and Kuruvilla's report which retrospectively studied charts of 200 patients.

4. IMPLICATIONS OF THE STUDY

This research has studied directly very important factors in the alcohol literature such as FH, AOO and Severity. While some Indian studies have begun to study such aspects, we attempted a study in that direction.

As both factors, namely age of onset and family history have been shown to correlate significantly with severity of alcohol dependence, we can state that these factors do play an important role in our population in spite of cultural and socio-demographic differences compared to western situation. This has implications for Biopsychosocial conceptualisation of Alcoholism.

As discussed above, whether these represent genetic contributions or impact of decidedly-generally-higher family influence in the Indian context remains to be explored. In the absence of carefully maintained Registers of Twins/Adoptees this can pose a major challenge for research

in the Indian context. On the other hand other studies looking at endo-phenotypes and outcomes of alcoholism may give some pointers in this direction. If one accepts family history of alcoholism as an index of heightened vulnerability, then its lowered correlation with Quantity-frequency sub-scale appears to emphasise physical withdrawal (core clinical feature) as a significant marker of the problem than routinely observable measures of actual intake.

FH & AOO has an independent effect on the severity. So it may be useful in educating the high-risk adolescents with FHP against the use of alcohol or atleast delay the use till a much later age.

5. LIMITATIONS OF THE STUDY

1. One of the important issue is whether this data is generalisable in our population, considering that this was done in an inpatient population of a Psychiatry Hospital, this sample may not represent the general population. Infact we have no definite information even with regard to the Socio-demographic profile of the Hospital inpatient population. However, the large sample studied and the similarity of results in a variety of studies across different countries with different methodologies, seem to indicate that this may be replicable even in a well represented subject sample. However, the skewing of the severity scores despite planning to the

contrary may have limited the generalisability of the data to less severe-but-still-heavy- users of alcohol.

2. The second issue was the use of severity scale, it would be better to use a tool which has been used in the Indian context, Validated and available in the regional/local languages for assessment. Further, the method of using the SADQ, which though meant to be a self report, was scored using an one to one interview format may affect the psychometric properties of the scale, especially when used for further analysis. For e.g. this may particularly affect the analysis presented with regard to the sub-scales.

3. There was no blinding of data collection. Even though we used the severity scale first and then assessed the dependent variables, there could have been personal biases especially in determining the age of onset.

4. This study also mainly focused on the alcoholism history in the first and second relatives of the subjects and did not focus on the other psychiatric conditions in them, whether alcoholism was primary or secondary due to other conditions (psychiatric) was not ascertained. Also, we have not included in our analysis the prevalence of alcoholism in siblings, uncles and aunts, although this information was available.

6. FUTURE DIRECTION

We have laid the foundation for further studies stemming from the observations in this study. We would like to follow up the subjects to see if the FHD/age of onset continues to have an effect on the Outcome.

- Further studies may use a better Severity measures such as Addiction Severity Index (ASI), which may look at severity in a more detailed manner.
- There have been early significant studies on Electrophysiological parameters and Platelet MAO in India; incorporating these could add more knowledge in the area of vulnerabilities to Alcoholism.
- Later children of Alcoholics of our subjects could be followed up for vulnerabilities such as Behavioural manifestations, reaction to ethanol, Platelet MAO activity and Imaging studies of the Brain.

SUMMARY AND CONCLUSIONS

The current study has attempted to:

1. Compared the SEVERITY OF ALCOHOL DEPENDENCE in two groups of problem drinkers divided on the basis of presence or absence of family history of alcohol use in the first and second-degree relatives.
2. Correlated SEVERITY OF ALCOHOL DEPENDENCE WITH FAMILY HISTORY DENSITY IN SUBJECTS with problem drinking
3. Studied the AGE OF ONSET OF ALCOHOL USE in subjects with problem drinking and to correlate this with SEVERITY OF ALCOHOL DEPENDENCE.
4. Further looked at the independent effects of FHD and AOO on Severity.
5. Also studied the association FHD on subgroups of SADQ measure.
6. We have shown that even in the local context, Family history of Alcohol related problems, Age of Onset and Severity of alcohol dependence in the index subjects all correlate significantly with each other. As far as we are aware this is one of the first Indian studies to

directly probe this relationship in a large enough sample of problem drinkers. The replication of this finding in a different culture like ours has implications for the Biopsychosocial conceptualisation of Alcoholism. Also, the role of Age of Onset of alcohol use needs to be further understood. This could open up opportunities for preventive efforts in this area. The study has limitations in terms of sampling issues and measures of Severity available for use in the local context.

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AUDIT questionnaire: screen for alcohol misuse¹

Please circle the answer that is correct for you

1. How often do you have a drink containing alcohol?

- Never
- Monthly or less
- 2–4 times a month
- 2–3 times a week
- 4 or more times a week

2. How many standard drinks containing alcohol do you have on a typical day when drinking?

- 1 or 2
- 3 or 4
- 5 or 6
- 7 to 9
- 10 or more

3. How often do you have six or more drinks on one occasion?

- Never
- Less than monthly
- Monthly
- Weekly
- Daily or almost daily

4. During the past year, how often have you found that you were not able to stop drinking once you had started?

- Never
- Less than monthly
- Monthly
- Weekly
- Daily or almost daily

5. During the past year, how often have you failed to do what was normally expected of you because of drinking?

- Never
- Less than monthly
- Monthly
- Weekly
- Daily or almost daily

6. During the past year, how often have you needed a drink in the morning to get yourself going after a heavy drinking session?

- Never
- Less than monthly
- Monthly
- Weekly
- Daily or almost daily

7. During the past year, how often have you had a feeling of guilt or remorse after drinking?

- Never
- Less than monthly
- Monthly
- Weekly
- Daily or almost daily

8. During the past year, have you been unable to remember what happened the night before because you had been drinking?

- Never
- Less than monthly
- Monthly
- Weekly
- Daily or almost daily

9. Have you or someone else been injured as a result of your drinking?

- No
- Yes, but not in the past year
- Yes, during the past year

10. Has a relative or friend, doctor or other health worker been concerned about your drinking or suggested you cut down?

- No
- Yes, but not in the past year
- Yes, during the past year

Scoring the audit

Scores for each question range from 0 to 4, with the first response for each question (eg never) scoring 0, the second (eg less than monthly) scoring 1, the third (eg monthly) scoring 2, the fourth (eg weekly) scoring 3, and the last response (eg. daily or almost daily) scoring 4. For questions 9 and 10, which only have three responses, the scoring is 0, 2 and 4 (from left to right).

A score of 8 or more is associated with harmful or hazardous drinking, a score of 13 or more in women, and 15 or more in men, is likely to indicate alcohol dependence.

¹Saunders JB, Aasland OG, Babor TF *et al.* Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption — II. *Addiction* 1993; **88**: 791–803.

SEVERITY OF ALCOHOL DEPENDENCE QUESTIONNAIRE (SADQ-C)¹

NAME _____ AGE _____ No. _____

DATE:

Please recall a typical period of heavy drinking in the last 6 months.

When was this? Month:..... Year.....

Please answer all the following questions about your drinking by circling your most appropriate response.

During that period of heavy drinking

1. The day after drinking alcohol, I woke up feeling sweaty.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS
2. The day after drinking alcohol, my hands shook first thing in the morning.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS
3. The day after drinking alcohol, my whole body shook violently first thing in the morning if I didn't have a drink.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS
4. The day after drinking alcohol, I woke up absolutely drenched in sweat.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS
5. The day after drinking alcohol, I dread waking up in the morning.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS
6. The day after drinking alcohol, I was frightened of meeting people first thing in the morning.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS
7. The day after drinking alcohol, I felt at the edge of despair when I awoke.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS
8. The day after drinking alcohol, I felt very frightened when I awoke.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS
9. The day after drinking alcohol, I liked to have an alcoholic drink in the morning.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS
10. The day after drinking alcohol, I always gulped my first few alcoholic drinks down as quickly as possible.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS
11. The day after drinking alcohol, I drank more alcohol to get rid of the shakes.
ALMOST NEVER SOMETIMES OFTEN NEARLY ALWAYS

¹ Stockwell, T., Sitharan, T., McGrath, D. & Lang, . (1994). The measurement of alcohol dependence and impaired control in community samples. *Addiction*, 89, 167-174.

12. The day after drinking alcohol, I had a very strong craving for a drink when I awoke.
ALMOST NEVER SOMETIMES OFTEN ALMOST ALWAYS

13. I drank more than a quarter of a bottle of spirits in a day (OR 1 bottle of wine OR 7 beers).
ALMOST NEVER SOMETIMES OFTEN ALMOST ALWAYS

14. I drank more than half a bottle of spirits per day (OR 2 bottles of wine OR 15 beers).
ALMOST NEVER SOMETIMES OFTEN ALMOST ALWAYS

15. I drank more than one bottle of spirits per day (OR 4 bottles of wine OR 30 beers).
ALMOST NEVER SOMETIMES OFTEN ALMOST ALWAYS

16. I drank more than two bottles of spirits per day (OR 8 bottles of wine OR 60 beers).
ALMOST NEVER SOMETIMES OFTEN ALMOST ALWAYS

Imagine the following situation:

1. You have been **completely off drink for a few weeks**
2. You then drink **very heavily** for two days

How would you feel the **morning after** those two days of drinking?

17. I would start to sweat.
NOT AT ALL SLIGHTLY MODERATELY QUITE A LOT

18. My hands would shake.
NOT AT ALL SLIGHTLY MODERATELY QUITE A LOT

19. My body would shake.
NOT AT ALL SLIGHTLY MODERATELY QUITE A LOT

20. I would be craving for a drink.
NOT AT ALL SLIGHTLY MODERATELY QUITE A LOT

SCORE

CHECKED BY:

ALCOHOL DETOX PRESCRIBED: YES/NO

NOTES ON THE USE OF THE SADQ

The Severity of Alcohol Dependence Questionnaire was developed by the Addiction Research Unit at the Maudsley Hospital. It is a measure of the severity of dependence. The AUDIT questionnaire, by contrast, is used to assess whether or not there is a problem with dependence.

The SADQ questions cover the following aspects of dependency syndrome:

- physical withdrawal symptoms
- affective withdrawal symptoms
- relief drinking
- frequency of alcohol consumption
- speed of onset of withdrawal symptoms.

Scoring

Answers to each question are rated on a four-point scale:

Almost never	- 0
Sometimes	1
Often	2
Nearly always	3

A score of 31 or higher indicates "severe alcohol dependence".

A score of 16 -30 indicates "moderate dependence"

A score of below 16 usually indicates only a mild physical dependency.

A chlordiazepoxide detoxification regime is usually indicated for someone who scores 16 or over.

It is essential to take account of the amount of alcohol that the patient reports drinking prior to admission as well as the result of the SADQ.

There is no correlation between the SADQ and such parameters as the MCV or GGT.

IDENTIFICATION DATA OF THE PATIENT

Name: Age: Sex:

IP/OP No: D.O.A:

Diagnosis: Address:

Sociodemographic details:

Educational status: No education/primary/secondary/diploma/ graduate

Marital status:Single/Married/Separated/Divorced/Remarried

Occupational status: Student/farmer/business/service/professional/retired

Income:

Family status: Nuclear/joint/extended/Living alone

ஆராய்ச்சி ஒப்புதல் கடிதம்

ஆராய்ச்சி தலைப்பு :

பெயர் :

தேதி :

வயது :

உள் நோயாளி எண் :

பால் :

ஆராய்ச்சி சேர்க்கை எண் :

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது.

எனக்கு விளக்கப்பட்ட விஷயங்களை நான் புரிந்துகொண்டு நான் எனது சம்மதத்தைத் தெரிவிக்கிறேன்.

இந்த ஆராய்ச்சியில் பிறரின் நிர்ப்பந்தமின்றி என் சொந்த விருப்பத்தின் பேரில் தான் பங்கு பெறுகிறேன் மற்றும் நான் இந்த ஆராய்ச்சியிலிருந்து எந்நேரமும் பின்வாங்கலாம் என்பதையும் அதனால் எந்த பாதிப்பும் ஏற்படாது என்பதையும் நான் புரிந்துகொண்டேன்.

இந்த ஆராய்ச்சியின் விவரங்களைக் கொண்ட மருத்துவ ஆராய்ச்சியில் என்னை சேர்த்துக் கொள்ள சம்மதிக்கிறேன்.

நான் என்னுடைய சுயநினைவுடன் மற்றும் முழு சுதந்திரத்துடன் இந்த மருத்துவ ஆராய்ச்சியில் என்னை சேர்த்துக்கொள்ள சம்மதிக்கிறேன்.

கையொப்பம்

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No : 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr.Hariharan. P
PG in MD Psychiatry
Madras Medical College, Chennai -3

Dear Dr.Hariharan. P

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "correlation between severity of alcohol dependence with age of onset and family history" No.06082012.


The following members of Ethics Committee were present in the meeting held on 10/08/2012 conducted at Madras Medical College, Chennai -3.

- | | |
|--|---------------------|
| 1. Dr. S.K. Rajan. M.D.,FRCP.,DSc | -- Chairperson |
| 2. Prof. Pregna B. Dolia MD
Vice Principal, Madras Medical College, Chennai -3
Director , Institute of Biochemistry, MMC, Ch-3 | -- Member Secretary |
| 3. Prof. B. Vasanthi MD
Prof of Pharmacology ,MMC, Ch-3 | -- Member |
| 4. Prof. C. Rajendiran, MD
Director , Inst. Of Internal Medicine, MMC, Ch-3 | -- Member |
| 5. Prof. S. Deivanayagam MS
Prof of Surgery, MMC, Ch-3 | -- Member |
| 6. Thiru. S. Govindsamy. BABL | -- Lawyer |
| 7. Tmt. Arnold Soulina MA MSW | -- Social Scientist |

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.


Member Secretary, Ethics Committee

Originality

GradeMark

PeerMark

Correlation of severity of alcohol dependence

BY HARIHARAN 20106303 M.D., PSYCHIATRY

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ALCOHOL DEPENDENCE WITH AGE OF ONSET AND FAMILY HISTORY

Dissertation submitted to the
TAMIL NADU DR. M. G. R. MEDICAL UNIVERSITY

in partial fulfillment of the requirements for

M.D (PSYCHIATRY)

BRANCH XVIII



APRIL 2013

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